THEORY AND PRACTICE OF THYROID THERAPY

WALLER

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Theory and Practice

OF

Thyroid Therapy

Being some experiences of the results of Thyroid medication, with deductions concerning the influence of Thyroid secretion in health and disease, and certain effects of drugs and various circumstances upon Thyroid secretion

A BOOK FOR GENERAL PRACTITIONERS

BY

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PREFACE.

In offering the following work to the consideration of the Medical Faculty, I wish to acknowledge my indebtedness to the numerous writers to whose works reference is made, and in particular to Dr. Leonard Williams, whose writings have been largely responsible for renewing my interest in this particular branch, which has always appealed to me as being worthy of special study. My aim throughout has been to collect facts, and also ideas and theories based on facts, by the careful consideration of which I have attempted to draw conclusions and so advance our knowledge on the subject. I have had opportunities of treating a considerable number of patients from the thyroid standpoint, with certainly more success than I should have anticipated. I am firmly convinced that some understanding of thyroid matters is essential to the practitioner in treating every case, and will materially improve his success in the treatment of fully one-fourth of his patients. I cannot venture to hope that my interpretation

of the facts and theories under consideration is in all cases correct. The science of thyroid therapy is like all other sciences, in which what we deem to be fact to-day may eventually have to be regarded in a different light. But it is given to some to climb to success by observing the mistakes of others. So if, here and there, I have fallen into some pit unawares, others may thereby be enabled to perceive the snare and keep out of it. On the other hand, I venture to think the account of my wanderings into this little-known land may prove interesting to all, and perhaps of assistance to some in enabling them to penetrate still farther. At present the literature on the subject of thyroid therapy consists for the most part of monographs of thyroid treatment in many and various diseases. Such solitary articles are read, some by one practitioner, some by another, and are passed over or retained according to the circumstances of the moment. As to the more advanced works on such complaints as Graves's disease or myxœdema, the general practitioner is apt to consider them for the most part outside his line. He has occasionally a case of either complaint, and enough general examination knowledge to give him rough ideas as to treatment. Whether he then follows up the subject, or not, depends as a rule on the

influence of the patient, and the general pressure of other work and interests at the moment. But I venture to say that few practitioners, and not all consultants, have any idea of the individual importance to them of even such an incomplete knowledge of thyroid therapy as I have here attempted to outline. I must also take this opportunity of expressing my gratitude to Mr. Rollinson-Whitaker, who has been kind enough to pass on to me for medical treatment some of his cases who were not at the moment within the realms of surgery, and has thus provided me with most valuable additional material for observation.

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THEORY AND PRACTICE OF THYROID THERAPY.

CHAPTER I.

Some Symptoms and Results of Thyroid Inadequacy.

THERE is a large and apparently utterly diverse group of diseases and ailments for which thyroid gland has been prescribed, often, it is feared, without any intelligent understanding of the objects to be attained, or how the process is to be arrived at. When one sees such a list as myxœdema, cretinism, obesity, puerperal eclampsia, simple goitre, exophthalmic goitre, psoriasis, lupus, eczema, cheloid, syphilis, tetany, hæmophilia, torticollis, acromegaly, ununited fracture, malignant disease, beriberi, certain diseases of the eye and ear, hæmorrhage from the uterus, mental diseases, backwardness of children, nocturnal enuresis, enlarged tonsils and adenoids, alopecia, and many more, one is at first sight driven to the conclusion that anyone who prescribes thyroid for such diverse conditions is thyroid mad, or else acts on the plan, "When in doubt, give

thyroid." And the list I have given is not exaggerated. I have quoted chiefly from one accessible to most general practitioners, including a few diseases from various articles I have read on the subject, and could extend the list considerably.

In the following pages I shall endeavour to discuss the subject from a rational point of view, so far as I have been able to elucidate the matter from my own observations and experience in a considerable number of cases, and also from a consideration of the views of many writers on various aspects of the influence of the thyroid on the body, and how thyroid activity may be affected by disease and different conditions of metabolism, and also by various drugs. The importance of this matter in practical medicine can hardly be over-rated, seeing that thyroid secretion is probably to a large extent responsible for many of the little details of daily life, the sum of which makes all the difference between being robust and delicate, enjoying life or being a martyr to various petty discomforts. Myxœdema and Graves's disease must be taken as the two extremes of thyroid secretion—myxœdema, of course, representing complete failure of secretion and Graves's disease the utmost excess. But, it is not too much to say that the intermediate conditions of thyroid

secretion are just as important as the two conditions just mentioned.

The minor degrees of thyroid insufficiency have been admirably described by Leonard Williams, in an article in *Folia Therapeutica* for October 1909, quoted in full in the *Medical Review*, May 1910. This article contains food for much thought, but to put the matter very briefly, Leonard Williams shows that one of the most important functions of the thyroid gland is that of fixing the calcium salts of the body. He points out further the relationship of thyroid activity to menstruation and pregnancy, and enumerates various minor signs of thyroid insufficiency, such as the presence of enlarged tonsils and adenoids, which are an attempt on the part of the organism to supply a secretion that is lacking. His evidence that nocturnal enuresis is due to failure of thyroid function is indisputable.

Other minor symptoms referred to are subnormal temperature, hyper-sensitiveness to cold, loss and scantiness of hair, premature greyness, dysmenorrhœa and periodical migraine, and excessive dental caries. And he also points out that thyroid depression is liable to follow any acute illness. Now many of these symptoms were well illustrated in a case under my own care, in whom thyroid extract worked marvels. The case is an extreme type of a

common variety. I made his acquaintance at the Dental Hospital. His initials were A. T., and his age was 6 years. He was a tiny little fellow only 3 ft. high, and weighing 28 lb. All his teeth were terribly decayed. He looked pale and ill, and his hair was very scanty. It was not difficult to elicit from his mother that the child was never well. She had in fact been taking him to hospitals (she named two well-known institutions) for several years regularly, and he had been taking a lot of cod liver oil, but she could not see that he was any better. All she had been told as to the nature of his malady was that it was rickets. Etiologically this was true, but the child was not in any way deformed, nor had he beaded ribs. His skull was of a rickety type, and he had a big belly, but no superfluous flesh on body or limbs. He was always fretful, cold and tired. She had great difficulty in feeding him, as he never wanted food. Water was the thing he craved for, and that to such an extent that he actually drank the water in which the flowers were placed at school. His mother was always endeavouring to keep the water out of his way, as otherwise he drank far more than she thought good for him. I had the quantity of urine measured on several occasions, but it was not excessive, a little over a quart in twenty-four hours, and contained

neither albumin nor sugar. He was a good deal smaller than his younger brother, aged 4, and the mother attributed his ill-health to the fact that, while pregnant, she was nursing his father through a serious illness for five months and was often short of food. Now thyroid tablets at the rate of 1¼ gr. to 2½ gr. a day worked wonders for this little boy. He became a happy child instead of a miserable one. His appetite improved to such an extent that his mother, a poor woman with four children, could appreciate the difference in the bread bills. He cried for his rice pudding. His thirst was much less, though at the time of writing, his mother tells me, he always asks for a glass of water when he comes down in the morning, and also as soon as he gets home from school. I have noticed this symptom of thirst in several other cases of thyroid deficiency.

He would now play contentedly in the garden in the coldest weather, though previously he was always cowering down by the fire. His hair commenced to grow, and had to be cut as often as that of other children. His colour improved immensely. He commenced to increase in height at the rate of ½ in. in six weeks, and had grown 1¾ in. in six months. I must lay stress on this growth, because he was 7 in. below the average

height for his age at the beginning of the thyroid treatment, and the average rate of growth for a boy of his age is 3 in. a year. He also increased duly in weight. His mother was naturally delighted, and loud in her affirmations of what her neighbours and the boy's school teachers said as to the evident difference in the child. Nor could there be any doubt as to cause and effect, because the drug was left off for a fortnight on several occasions during the earlier stages of treatment, and the child was never so well when not taking it, improvement immediately following when he resumed it. He has also been able to take advantage of his calcium supply, as evidenced by the fact that his first permanent molars and his central incisors have now erupted, and appear to be all that could be desired, though, as already mentioned, the whole of his temporary teeth were carious.

Now the importance of this function of the thyroid gland in enabling the body to make use of calcium salts can hardly be over-rated. The hall-mark of rickets of the fully-developed type is, I suppose, the obvious deficiency of calcium salts in the bones, and the resulting deformity, though this is still further enhanced by weakness of ligaments and muscles.

And while many of the symptoms already referred to as marks of thyroid deficiency are

present in nearly every case of rickets, it is the "rickety" condition of the skeleton that gives the name to the disease, whether we accept the Anglo-Saxon or the Greek etymology of the word. Probably there is hardly a medical man who has not at some time prescribed calcium in some form for such a case, only to be disappointed in the results. I find, however, that Treves's "System of Surgery" says, "The administration of phosphate of lime is of little use, being mainly excreted in the urine, a proof that *want of power to assimilate the lime salts* is rather the cause of defective ossification than deficiency of lime salts in the diet."

I think that anyone who will investigate the evidence already to hand and pursue the subject further on his own account, cannot fail to be convinced that the connecting link is, as Leonard Williams insists, the activity of the thyroid gland.

The condition of rickety children of course varies, but the matter is not difficult to explain on this assumption as to the etiology.

One child may still show all the symptoms of thyroid insufficiency already enumerated. In another, the thyroid gland may have recovered itself, and only left results of the damage already done. In such a case we may suppose that some debilitating cause has been

at work, and by upsetting thyroid secretion has induced a calcium famine of longer or shorter duration. Accordingly, the softened bones yield and various results occur—crooked limbs or spine, or contracted pelvis, or pigeon breast—according to the nature of the strain that is put on the inadequately calcified bones, and also according to the longer or shorter duration of this thyroid inadequacy.

Personally, however, I am of opinion that rickets in its worst form, starting as it then does in the earliest months of life, is primarily caused by depriving the infant of the benefit of *maternal* thyroid activity, the infant's own thyroid secretion being invariably unequal to its requirements at birth. This most interesting subject will be fully discussed further on.

The association of pigeon breast with enlarged tonsils (adenoids were nothing accounted of apparently) was first noted by Dupuytren about 1826, and this combination of maladies has been duly set forth in the text-books ever since. But in those days probably only extreme cases were noted, as it was no unusual thing to wait two or three years "till the child was better able to stand the operation." Nowadays, I venture to say the proportion is exceedingly small. And when pigeon breast occurs, I suggest that probably some other factor has been at work, such as hooping-cough

or laryngismus stridulus. The latter disease is a special perquisite of rickety children, and it is only natural that the uncalcified bones should yield under the strain. But it has already been mentioned that enlarged tonsils and adenoids are a confession of thyroid inadequacy on the part of the organism, so we need not marvel if they are put into the pathological picture, which after all only represents some of the various phases of the rickety type. The moral of this is, that when you remove the tonsils and adenoids you must be prepared to give thyroid. But an amazing benefit seems sometimes to accrue to a child as the direct result of the operation. I have wondered whether suddenly depriving the system of this added secretion has not in these cases acted as a powerful stimulus to the thyroid gland. The gland, at one time, unable to secrete sufficiently, was helped by Nature, who provided a substitute, a harmful one no doubt, but still a substitute. So the thyroid took a holiday and got well, but finding the substitute there, had no need to work. When, however, the substitute and its wickedness were removed, the thyroid, now fully capable and under sufficient stimulus, stepped into the breach, and all was well.

But nowadays the ever-watchful surgeon has usually removed the tonsils and adenoids,

almost as soon as Nature has accomplished their development, and the thyroid, not having had any assistance is unready for work. In such cases a little well-directed thyroid medication is obviously indicated. As a matter of fact, however, those with enlarged tonsils and adenoids are presumably less liable to suffer from calcium famine than those without. The secretion is worth something in spite of its pathological origin. This, as Leonard Williams has shown, is proved by the fact that other symptoms of thyroid inadequacy, such as nocturnal enuresis, may become worse after the removal of the tonsils and adenoids, and also by the fact that administration of thyroid causes atrophy of these pathological substitutes. But if pigeon breast is not now so commonly associated with tonsillar hypertrophy and nasal obstruction as formerly, it must be conceded that the sufferers are prone to have narrow and flattened chests. This may be partly the result of obstructed inspiration, but is probably rather due to the action of the diaphragm pulling the unduly yielding ribs inwards, as it contracts during inspiration. But there is, I think, yet another factor. Children with big tonsils and adenoids commonly exhibit another feature of thyroid insufficiency, namely, hypersensitiveness to cold, so they unconsciously adopt the attitude of

greatest self-protection—namely, with the shoulders and arms thrown forward and a slight stoop. One never sees a man, shivering with cold, yet with head erect and chest expanded, except perchance a soldier on parade. The lateral pressure of the arms on the chest and the generally huddled up position of the shivering child is bound to produce its effect if long continued during the growing period, especially when the bones, though not so soft as in a case of well-marked "rickets," are probably, to some extent, deficient in lime salts.

There is another common deformity so frequently associated with enlarged tonsils and adenoids that for a long time it was thought to be a natural result. I refer to the high palate, in which condition the cavity of the mouth encroaches on that of the nose, thus lessening the facility of nasal respiration and imparting a peculiar tone to the voice by interfering with the efficiency of the hard palate as a sounding board. Leonard Williams, however, points out what has also been noted by other observers, that many patients who have the high arch are free from enlargement of the tonsils and presence of adenoids, and he tells us that StClair Thomson has observed that the palates of children whose tonsils and adenoids he removed have even become increasingly arched after the operation. We are driven to

the conclusion, therefore, that the deformity is due to yielding of the bones under some stress, just as other deformities are produced in rickets. In short, the primary cause is thyroid insufficiency, which involves calcium deficiency. I am not well enough up in the mechanics of the jaw to say what stress may be present which could cause the palate to yield when insufficiently calcified, but I suggest that it might be the pressure of the tongue in the act of swallowing. One can readily imagine that if the mouth is habitually used as an air-passage instead of the nose, there is at least no encouragement to the development of a free nasal passage. Also, if the mouth is practically never shut there can be no effective upward pressure of the teeth of the upper jaw by those of the lower, which pressure would tend to flatten out and spread the palate. But neither of the latter factors could be responsible for the origin of a high palate in the absence of nasal obstruction, which is not always present, though they might well require attention when attempting to correct the deformity. It has been pointed out by Leonard Williams in the paper already referred to, that many cases of rickets, enlarged tonsils with adenoids, and nocturnal enuresis will be found on inquiry to have dated from one of the infantile febrile diseases, which has induced in

the first case what I have termed a calcium famine; in the second a pathological attempt at compensation; and in the third a condition not so easy to explain, but one for which, in the majority of my own cases, thyroid gland has proved itself the specific that Leonard Williams claims it to be.

CHAPTER II.

Causes of Increase of Dental Caries and Thyroid Insufficiency.

I NOW wish to show that this calcium famine in a minor degree almost invariably occurs as a sequel of the febrile diseases of childhood, and that in the form of dental caries. Dental caries is a subject of vast importance, and one which is being discussed all over the country at present, though I have not heard any mention of thyroid gland in the discussions; but as Leonard Williams points out, an undue amount of dental caries should always excite a suspicion of thyroid inadequacy. This point was well shown in the first case quoted.

It is now some fourteen years since a London dentist—then in the first ranks of his profession, now, I regret to say, dead—taught me that it is very common to find symmetrical decay of the permanent molars, perhaps especially the "sixes," as the result of measles or some other child's complaint occurring shortly before or soon after their eruption. And many times I have observed the truth of this fact, and also gained to myself credit

for great intuition by a judicious inquiry based on this assumption. I see no reason why the same should not hold good for the other teeth. The molars are of course larger and require more nutriment, and are therefore more likely to be affected by this transient calcium famine —the result of thyroid depression.

Now let us turn for a moment to Smale and Colyer's authoritative work on diseases of the teeth. "In endeavouring to ascertain the cause (of the increase of dental caries) it may be interesting and instructive to remember that the teeth have not alone suffered, marked deterioration having taken place in other organs, as evidenced by the increase of defective eyesight and tendency to hypertrophy of adenoid tissue in the naso-pharynx." It is indeed "interesting and instructive," inasmuch as thyroid inadequacy is responsible both for caries and adenoids. We see here, I think, the influence of universal education in spreading the minor infectious complaints, and incidentally also in producing, or perhaps sometimes only making evident, defective eyesight.

Our inquiry into the cause of increased dental caries is therefore now resolved into another question—namely, What is the cause of the decrease of thyroid activity? I have just given one answer to this question —

namely, the spread of infectious complaints in childhood inseparable from universal school education. The schools are undoubtedly the happy hunting ground for the germs of measles, scarlet fever, diphtheria, hooping-cough, mumps, and such like. Doubtless, prizes given for uninterrupted attendance contribute towards this spread of infection, as many scholars are thereby induced to attend school during the early and highly-infectious period of such a disease as measles. The rash is not observed till about the fifth day, and in a mild case an enthusiastic child could easily stand out against the initial symptoms. The same applies for a shorter period to the initial sore throat of scarlet fever or to diphtheria. Also to the early stage of hooping-cough. And not only the attendance prizes are at fault, but also the continual harassing of attendance officers, however worthy the object. The present position is that parents are afraid to keep a child from school if it is possible for him or her to get there. Unless a doctor's certificate be forthcoming, there is likely to be trouble. A doctor's certificate may mean expense, and unless the child is obviously ill, the mother does not know that the certificate will be forthcoming. So, instead of waiting to see, she thinks she will be on the right side by sending the child to school. The school

is closed as a rule when about half the scholars have succumbed to the epidemic that ensues. Measles is a particularly common antecedent of adenoids.

Another reason for the increase of dental caries may perhaps be found in the loss of lime salts involved in the modern preparation of flour. This suggestion is the one commonly favoured, I believe, by the dental profession. I suggest, however, that it is not merely the loss of calcium, *per se*, that is the cause, but the fact that in this loss of lime the normal stimulus to thyroid activity is removed. As to the flour. It is now crushed between steel rollers, and refined in such a way that we are deprived almost entirely of the husk and germ of the grain with its valuable mineral constituents. In the old-fashioned way, part at least of this husk was pulverized between mill stones. Incidentally, we also lose the detritus from the mill stones themselves, but I do not know whether it is suggested that this loss is a harmful one.

I do believe, however, that calcium salts are the normal stimulus to thyroid metabolism, and without this stimulus secretion may become deficient. In this connection it may be interesting to quote from Ringer and Sainsbury's "Therapeutics," a work of acknowledged authority: "Experience has

shown that lime water or carbonate of lime is a valuable remedy in deficient nutrition, and in convalescence from various diseases, its good effects being most marked in children suffering from rickets, malnutrition, &c. . . . One point may be noticed here, confirmed both by theory and experience—namely, that small doses will do as much good as large ones." Now the cases here described correspond exactly with those of thyroid deficiency. And the small doses referred to are sufficient to act as a stimulus without overtaxing thyroid activity, so benefit follows. I think that this thyroid-stimulating action of calcium is the explanation of the fact (also quoted in Ringer and Sainsbury's "Therapeutics") that "saccharated solution of lime does not confine the bowels, but on the contrary relieves constipation." Lime-water mixed with milk often appears to keep the bowels regular in infants who otherwise have required aperients. I had an adult patient who suffers from chronic constipation while living in a district supplied wholly with soft water, in spite of the fact that he gets plenty of exercise. If, however, he goes to London, where he takes less exercise but drinks the hard water, his bowels are regular at once; and the same thing occurs in another district which happens to be chalky. We discussed everything else which could bear

on the subject, but could find no other reason for this curious anomaly. I have had no opportunity of investigating the matter further, but may add that he has other stigmata of thyroid inadequacy besides constipation — namely, hypersensitiveness to cold, and also that he is comparatively bald, though only about 36 years of age. On the other hand, many people become constipated at once on arriving in a hard-water district. Here one may well suppose that the thyroid is not in a condition to respond to the stimulus. Perhaps it is already putting forth all the secretion of which it is capable for the time being. Obviously, then, if some be neutralized there will be a deficiency, and some sign of thyroid inadequacy will occur. I favour the above explanation on the ground that it seems highly improbable that the relatively small amount of calcium, even continuously taken in hard water, should cause constipation by acting as an astringent, especially in view of the fact that the opposite results sometimes occur. But the small amount of thyroid which we suppose might thus be neutralized would otherwise be a most potent agent in preventing constipation. So far as this symptom is concerned I have had almost invariably good results, and have only failed two or three times to cure constipation by the administration of thyroid. The

successes have been numerous, but do not present any special points worth recounting. My most marked failure was in a child of 18 months, who became obstinately constipated when cutting teeth. The same thing happened several times, and though probably due to thyroid exhaustion, as evidenced in several other ways, did not respond to even 2½ gr. three times a day. Small doses were of course tried first, and one did not care to exceed the quantity named. One must bear in mind, however, that thyroid is not a purge, and will not act as such. The bowels must be well opened at first, and then there is every chance that thyroid will keep them regular.

This preliminary clearance is a very important point, and was probably the cause of failure in the case of the infant just referred to, because in her case even large doses of aperients were not really effective, so possibly we never gave the thyroid a fair chance. But when the offending tooth was erupted constipation ceased to trouble. The cases most likely to be benefited are obviously those that show some other symptoms of thyroid inadequacy, and these often give remarkable results. But even in these cases, if the administration of thyroid does not correct constipation in a perfectly satisfactory manner within a few days, other measures must be taken for a time. I

feel pretty sure that the "vicious circle" plays an important part here. The endotoxins absorbed from fæcal accumulations make still further demands on the already insufficient thyroid secretion and in turn constipation is promoted by thyroid exhaustion.

Of course I do not wish to suggest that the cause of constipation is always thyroid exhaustion, though I do believe that this is the case far more often than is generally supposed. And it will not unfrequently be found that thyroid is the most potent agent in just those cases which have proved most refractory to the ordinary remedies. But as the subjects of thyroid insufficiency, in common with the rest of us, are subject to all the other various causes of constipation, it follows that thyroid cannot be looked on as a panacea, though it often gives remarkable results, and will frequently be found a useful adjuvant in other modes of treatment. Such, for instance, was a recent case of syphilis who was taking 1 gr. each of grey powder and Dover's powder five times a day. It was found that the patient though progressing admirably in all other ways was constipated, the bowels acting naturally about every three days. The patient was therefore allowed vegetables, fruits and soups, which so commonly have to be withheld, but that did not improve the condition. But I found that 2½ gr.

of thyroid daily kept the bowels perfectly regular. The dose could be omitted with impunity once in four days, but not oftener. It is of importance to avoid setting up diarrhœa in a patient undergoing a course of mercury, so the thyroid was really of value apart from the question of how far secondary syphilitic symptoms may be adversely influenced by thyroid depression. But to return to our calcium. We are deprived of lime by drinking less water than in the days of old. Doubtless the spread of the knowledge of germs has contributed much to this end. Many people never drink unboiled water at all. It is taken in the form of tea, coffee, cocoa, beer or some other concoction, and most of the calcium has been precipitated. Nevertheless, the influence of calcium is easily traced in those districts where a hard-water supply prevails, particularly in the rural districts where people lead a less artificial life, and are more likely to drink the beverage provided by Nature. In Smale and Colyer's work on dental caries, we find quoted the investigations of Röse *re* the influence of lime on caries.

Briefly, it was found that there was a much lower percentage of caries amongst the children who lived in a hard-water district than those living only a few miles away but drinking soft water. Now I think the influence of calcium

on thyroid activity is discernible in the figures there quoted. Firstly, there was a group of children who had an abundant calcium supply. They would be subject to any beneficial influence of having their thyroids stimulated daily by this calcium, and they had plenty of calcium if able to make use of it. What do we see? A percentage of diseased teeth over 16 and a percentage of children affected by caries, 79 in hard-water districts of Baden, 82·8 in those of Thuringia. This is a very high percentage of caries, so it follows that neither the presence of abundant calcium nor its stimulating effect on the thyroid gland were able to act as an efficient defence against dental caries. But such a result is not to be expected, because these children doubtless suffered from measles and other complaints productive of thyroid exhaustion and dental caries, and some would no doubt suffer from congenital thyroid inadequacy (without necessarily being cretins), because their parents had goitres, which are always more or less prevalent in hard-water districts. Others might suffer from thyroid exhaustion promoted by excess of calcium, and, again, rickets would contribute a certain number of cases. So the final result is a seriously high percentage of bad teeth, in spite of an abundant supply of calcium. Now turn to the other group of

children. The percentage of carious teeth is more than double and the percentage of children affected was 98·7 in soft-water districts of Baden, 92 in similar districts of Thuringia. In this group the causes of thyroid depression would operate in precisely the same way as in the other group, with one exception—namely, that the element of thyroid exhaustion due to *over*-stimulation by calcium and inheritance of a goitrous parentage would be eliminated. This elimination would of course affect the figures favourably rather than otherwise, decreasing the possible causes of caries. The great increase of caries in this group is therefore rightly attributed to the absence of the beneficial influence of lime. But it seems probable that even in soft-water districts the ordinary food would contain far more than the small amount of calcium required to make good the caries in these defective teeth, so that the real explanation is more likely to be that the caries in these children was due in some measure to a lessened efficiency of their thyroid glands caused by the greatly-lessened supply of the normal stimulant calcium, which would occur not only in the drinking water but also in vegetables and fruits grown in the districts. But an actual deficit of calcium is probably impossible, and it seems probable that dental caries, like rickets, is due to a greater or less

disability to absorb the calcium provided, owing to inefficiency of the thyroid gland — the medium through which such absorption is normally carried on. The influence of calcium on the thyroid will be further discussed in a later chapter devoted specially to this subject. The practical outcome of these considerations must naturally be the administration of thyroid substance to children whose first teeth have been unduly carious, in the hope that the second dentition may be favourably influenced. So far I have only been able to watch results of this procedure in two or three cases, and as far as can be said in so short a time it has answered admirably. But more prolonged evidence in a larger number of cases is necessary before one can claim that the result is more than a coincidence, perhaps dependent on other factors. It may be objected by some that in many cases the teeth are already calcified in the gum, though not erupted. True, but the teeth are still immature and it is necessary for their perfect development that there should be both an adequate supply of calcium and also power to absorb it.

Another cause of the increase in thyroid deficiency, and therefore indirectly in the increase of dental caries, may be found I think in the lower birth-rate and increasing disability of mothers to suckle their infants. The grow-

ing tendency of the day is to avoid not only lactation but pregnancy. The increased employment of female labour and the more artificial and strenuous existence of women in the higher social grades, coupled with increasing financial difficulties, are doubtless in a large measure responsible. As a consequence there is less demand for one of the thyroid functions. For this gland always enlarges and shows signs of increased activity during pregnancy and lactation. It is a law of Nature that an organ not fully made use of degenerates. A long family is, I think, in itself a proof of thyroid activity. As an illustration I may quote the case of Mrs. C.: She was married at the age of twenty, and had seventeen pregnancies in twenty years; four resulted in miscarriages, and thirteen children were born (no twins), of whom eleven are alive and in good health. She suckled all her children and had no difficulty in providing enough milk for them except with the last three. Surely, we may pardon her thyroid for being a little exhausted after such heroic efforts. But it has quite recovered itself now, for Mrs. C. is $64\frac{1}{2}$ and is remarkably devoid of the various stigmata of thyroid insufficiency. She has a beautiful head of hair down to her waist, thick and only just turning grey. Her eyebrows also are good; her bowels perfectly regular.

She does not like a hot-water bottle or many clothes on the bed. She likes cold water to wash in. She prefers cold weather to hot. She has no superfluous fat. She weighs 7 st. 12 lb., has plenty of energy and does most of her own washing. She has no skin troubles, and does not suffer from chilblains. She has no thyroid enlargement. Her neck is $11\frac{3}{4}$-in. round. She used to have a good set of teeth, but broke many in an accident when not quite 50 years of age. She has ten left now, which really is not so bad at $64\frac{1}{2}$ after seventeen pregnancies. The only thing she has had any real trouble with is headaches. But she has 4D of hypermetropia in one eye and 3D with ·5D of astigmatism in the other, and has only worn spectacles three years, so we cannot blame her thyroid for that. So far as I have been able to ascertain, Mrs. C.'s children have been endowed with special advantages which one may not unfairly attribute to the thyroid activity of their mother in the first instance, inasmuch as she was able to suckle them, and later to the fact that in thyroid matters they had a goodly heritage. Firstly, they all had good teeth. This is the mother's statement, and I have not been able to verify it. But it was given in good faith, and must at least be taken to imply that there was no excessive dental caries. That the front teeth appeared

sound, and the back ones were not decayed enough to cause toothache or dyspepsia and so draw attention to their condition. Secondly, they were remarkably free from the ailments of childhood. Except perhaps for an occasional bottle of medicine administered for some affection so trivial as to escape recollection, they had no medical attention. The mother is quite definite about this. The first doctor's bill she had to pay was for hooping-cough, with which the fourth child was affected at the age of 10 years. So far as fertility goes, two married daughters each have become pregnant twice in roughly four years' married life, and Mrs. C., has twelve grandchildren. The evidence so far as available is all in favour of thyroid activity being passed on to the next generation. I have omitted to mention that none of the children were operated on for enlarged tonsils or adenoids, nor did any of them suffer from nocturnal enuresis.

I have now given three reasons for increasing prevalence of dental caries, all operating through the thyroid gland :—

(1) Spread of measles and other "minor" infectious complaints through increased education movements.

(2) Loss of calcium salts in food and water, operating partly *per se*, but chiefly by adverse influence on thyroid activity.

(3) Decrease of thyroid activity due to loss of function entailed by evasion of maternity or lactation, or both.

The third of these reasons may now be considered at length, particularly in its bearing on rickets, to which I will respectfully draw the attention of the dental faculty and request them for the time being to look at caries from the point of view that dental caries is in many cases dental rickets.

CHAPTER III.

Thyroid a valuable Ingredient of Mother's Milk.

I HAVE already expressed an opinion that rickets, in its protean form, is caused by depriving the suckling of the benefits of maternal thyroid activity, which would, in the natural course of events, be obtained while at the breast. The same arguments apply in considerable measure to dental caries, and the two subjects are therefore interwoven. Dental caries is far less prevalent among savage races than our own. I have no doubt this is due, at least in part, to the fact that they nurse their children, thus both helping to maintain the thyroid activity of the race as a whole, and conferring the benefits of individual thyroid activity on the infants, while patent baby foods and feeding-bottles are absent, though I suppose they are making inroads like the rest of civilization. In the animal kingdom, also, dental caries is the exception rather than the rule, and I suggest that the reason here is the same—namely, that they suckle their young. On the other hand, of course, the laws of heredity and "the survival of the fittest" have their influence—con-

siderable among savage men, absolute among savage beasts. Any with thyroid deficiency, whether manifested in the form of dental caries, or rickets, or any other malady, would soon be wiped out. This would apply especially to the carnivora, so far as teeth are concerned, inasmuch as those with the best teeth would be victorious in the fights not only for food but also for the females. And amongst the herbivora, any with unsound teeth would not be able to graze in comfort, and would doubtless soon fall ill and die off. Similarly amongst animals, those who become victims of diseases such as might be supposed to cause thyroid depression, and thus give rise to dental caries, as measles does in children, would generally die under natural conditions, or be killed off by the stock-keeper as unprofitable to keep, so one could hardly expect often to see dental caries, thus arising amongst them. It is different with the human race. Though always striving to better our condition, we do much that is harmful to the race as a whole. Our poor efforts so often result in the preservation of the unfit—for a time at least—long enough for them to propagate their kind and pass on their unfitness to the next generation. Our business is to trace the origin of this unfitness if possible, and, as far as may be, strive to counteract, even if we are unable to eliminate it.

I think it may be fairly shown, then, that this loss of breast-feeding is a factor of grave importance. So far as dental caries is concerned, "Dr. Kingston Barton found during twenty years' experience that breast-fed children have the best teeth, those fed on cow's, ass's, or goat's milk coming off next best, but that when starch or patent foods were given in place of cows' milk, the teeth, both deciduous and permanent, turn out badly." The nursing mothers have active thyroid glands, for it has been shown that, if thyroid secretion be deficient or absent, a mother cannot continue to suckle her child. Also the administration of thyroid gland substance in such a case promotes or increases the flow of milk. Thus breast-fed children start in life with an inherited tendency to thyroid activity, in spite of any subsequent depression that may occur as the result of measles or other complaint. But I have no doubt that the suckling babe gets the benefit of its mother's thyroid secretion, acting through the milk, during the early months of life. In support of this contention I will quote a recent case. Mrs. B. had a much enlarged thyroid gland, and was nursing her baby, which was well and thriving. But, having to go out to work, she weaned the baby and put it on artificial food. Shortly after, the child developed urticaria, of the type known as "urticaria

chronica infantum." So far as one could see, this was not due to digestive troubles. The child was not sick, the bowels were regular and the motions a good colour. So, when looking for a cause, it occurred to me that perhaps the child was missing the mother's thyroid secretion. Accordingly I administered ½ gr. of thyroid extract to the baby twice a day, with excellent results. The spots rapidly got well. The mother accordingly left off giving the powders, with the result that a fresh crop of spots appeared. Administration of the powders was again effectual, so I think one must accept the inference.

Since writing this I have seen several other cases of this type of urticaria, accompanied by some other symptom of thyroid inadequacy, and thyroid treatment was speedily successful in all.

The protective influence of breast-feeding against rickets has been placed beyond dispute. It is said that rickets is prone to occur in the younger members of long families. If this be so, the fact is easily explained on the ground of thyroid exhaustion. If natural exhaustion were not likely to result, there are several other factors. The children bring their worries with them, and a mother with half a dozen or more children is sure to have some incidental trouble or anxiety, perhaps some illness or

accident to one of the number, or worry as to some circumstance affecting their welfare, or perhaps she has some illness herself. Any factor such as these may depress her thyroid activity for a time, and the result may affect the baby at the breast or the infant yet unborn. The little boy whose case I first quoted owed his condition primarily to the illness of his father. For during five months before he was born his mother had great anxiety on that account.

It often happens that a mother is able to nurse all the earlier members of her family at the breast, but the supply partially or wholly fails when she has brought forth her "quiverful."

I feel quite certain also that deprivation of breast-feeding has a very material influence in the production of adenoids and enlarged tonsils, and, in short, of most of the symptoms of minor thyroid inadequacy with which one meets in childhood. So far as I have been able hitherto to collect evidence on this point, I find that these subjects nearly all fall into two groups. Those that have had measles comprise about half the number, and the majority of the other half prove to have been bottle-fed. Some, of course, come under both these headings. It appears that measles is about the commonest and most potent cause of thyroid inadequacy, and I find that where a second

operation for removal of tonsils or adenoids has been necessary the victim has not infrequently had an attack of measles between the two operations. This is a point of considerable importance both for the patient and the surgeon. If a second operation is needed, the surgeon usually gets blamed for not having done the first one properly. But this is not necessarily the case at all. It is the business of the surgeon to remove the adenoids and leave behind the mucous membrane, which is the natural lining of the pharynx. So long as the mucous membrane remains, it is possible that the lymphoid tissue which it contains may again hypertrophy and produce adenoids. The determining factors will be, on the one hand, the continuance or otherwise of the thyroid insufficiency which first called the adenoids into being, and, on the other, the natural recuperative power of the child, which enables it to develop its own resources when thyroid secretion is in abeyance.

As to tonsils, it must have occurred to every surgeon of experience sometimes to meet with a second enlargement after a technically perfect operation. Personally, it has fallen to my lot to remove enormous tonsils twice from the same child, about a year intervening between the two operations. If, however, the first operation be followed by an adequate course

of thyroid, neither tonsillar enlargement nor adenoids are likely to recur. But, leaving measles out of the question, in the other group were many children who seemed always to "do badly," though no particular cause was apparent. These mostly proved to have been bottle-fed, and one must assume that they started life without any maternal thyroid assistance, and never quite caught up in thyroid secretion. These cases are common enough, and when treated with thyroid furnish most gratifying successes. They have generally been medically examined, and nothing definite has been found. The parents have cherished the hope that at 7 or 10, or some other particular age, the child would get on.

It is perfectly astonishing what changes can be wrought with a few months' attention and the use of thyroid, arsenic, calcium and iodides, one or all and in varied combination, the main factor being thyroid. I have been accustomed to weigh my cases as often as possible, and the steady increase of weight, the improved appetite, regularity of the bowels, disappearance of excessive thirst, and general improvement in the nervous disposition of the child are a treat to behold. The last such case I have seen at the moment of writing has gained 7 lb. in four months and a half. The average increase for his age during that time would

have been not quite 2 lb. He is still a trifle under weight for his age, but will soon catch up if he maintains his present progress.

I have just said that dental caries is relatively rare among uncivilized races, and in the animal kingdom as distinct from the human race. The same is true of rickets and the same arguments apply with almost double force. Cheadle, with a vast experience, is only able to quote one case of rickets arising in a child while at the breast during the first ten months of life. In that particular case the mother became pregnant during lactation, so I suggest that the unborn infant claimed most of her thyroid secretion, and did not leave sufficient surplus to be excreted in the milk. The same authority, in conjunction with Bland Sutton, made some most interesting observations among wild animals at the Zoological Gardens. The observations may be found in Clifford Allbutt's "System of Medicine." Briefly, the facts are that young animals deprived of their mother's milk commonly die of acute rickets. Many litters of lion cubs have so perished; also young bears and monkeys. Rickets is also dreaded by every breeder of large dogs if brought up "by hand." Young monkeys, deprived of their mother's milk and fed on vegetable food—chiefly fruit — became rickety. Two young bears fed on rice, biscuits, and raw meat, which

latter they hardly touched, died of extreme rickets. Young lions fed on horse flesh, and one additional meal per week of lean goat's flesh, died of extreme rickets; and Cheadle also remarks that children fed on oatmeal, corn-flour, bread, and patent foods, with little or no milk, certainly become rickety. The evidence here is conclusive that the essential cause of rickets is deprivation of some ingredient contained in the mother's milk. Now it was found possible to save the young lions by giving them a diet of milk, pounded bones, and cod liver oil, in addition to the raw meat diet, which without such additions proved fatal. Other conditions were the same and the cubs soon lost all signs of rickets aud grew up strong and healthy. Cheadle lays special stress on the influence of animal fat in the prevention of rickets. He adduces as further evidence the curative power of cod liver oil in rickets, and quotes M. Remy, who states that in Japan, where oils of fishes enter largely into food, and children are kept partly at the breast up to 5 years of age, rickets appears to be unknown.

In view then of the theory that thyroid insufficiency is the essential cause of rickets, let us review our facts. The young, when fed on the mother's milk, do not get rickets. During lactation there is evidence of increased maternal thyroid activity, and it is only natural

to suppose that the milk should in some way be the recipient of this increased activity. Further, as the milk is provided by Nature solely for the benefit of the young, it is only natural that this thyroid-born ingredient should be not only beneficial, but essential to health. Now the human infant, if fed on skimmed milk (cow's), is apt to become rickety. The inference is that the thyroid derivative is present more particularly in the cream or fat of the milk. Human babies, under otherwise normal conditions, thrive better when breast-fed than when given cow's milk, however carefully the latter be modified. But cow's milk, being so much richer in casein than human milk, is generally diluted with twice its bulk of water (lime-water or barley water) before the newborn baby is able to digest it. It follows that any thyroid substance contained in the cow's milk is thus diluted threefold before the babe has a chance of ingesting it. When cream is added to this diluted milk the child thrives better, probably because it is getting a better portion of the thyroid ingredient. The addition of the cream also makes cow's milk more closely resemble human milk, inasmuch as the latter is richer in fat, but I suggest that the value of the fat is largely due to its thyroidal content, inasmuch as an infant can easily manufacture its own fat out of carbohydrate material,

and therefore it is difficult to see why merely diminishing the supply of ready-made fat should be fraught with such a serious disorder as rickets. As to the diet of the young lions, they were deprived of their mother's milk with its thyroid potentialities; they died when fed on old horse meat. The old horse's thyroid was probably pretty well exhausted, youth being the period of greatest thyroid activity. Also we must assume that lean meat is at any rate not rich in this thyroid ingredient, if it be present at all. The addition of milk, crushed bones and cod liver oil was effective. The potentialities of milk have already been discussed. I do not know whether the milk of the lioness has been analyzed; but if it resembles that of another carnivore—the she-dog—one can readily suppose that cow's milk would be a very poor substitute. Bitches' milk contains about three times the quantity of casein and more than twice the fat found in cow's milk, and attempts to bring up puppies from birth on cow's milk usually end in failure. However, even for a lion's cub, cow's milk is doubtless better than no milk at all. As to crushed bones, if the thyroid gland be of paramount importance for satisfactory ossification to occur, it is at least possible that the bones may actually contain some thyroidal substance in a condition capable of being utilized by the young

animal. Perhaps the essential lime salts in the vitalized condition in which they are contained in fresh bone might be of some nutritive value in preventing the occurrence of rickets, though these same salts, it must be observed, are comparatively useless in this respect either when given in vegetable combination or crude chemical form. Lastly, there is cod liver oil, long recognized as the best weapon we have wherewith to combat rickets. I cannot help thinking that the iodine content of cod liver oil is the essential factor here, and able, in some measure at least, to replace the iodine content of the thyroid gland. The same argument applies to the case of the Japanese children, who are suckled late and fed on fish oils, which are almost certain to contain iodine. In treating rickets, however, in the human subject cod liver oil is not always so effective as it proved in the case of the young lions. This is probably a question of digestion. Many children can only tolerate quite a small and possibly insufficient dose to provide the necessary quantity of the iodine ingredient. In these cases, probably thyroid-gland substance would be more efficacious, as it proved in the case of the child, A. T., first quoted. If, as seems probable, the cream or fat in the mother's milk contains the thyroid ingredient, deprivation of which causes rickets, it is not to be wondered at that this

complaint and other minor degrees of thyroid insufficiency are so common among the children of the poor. When cow's milk is diluted to contain the same amount of casein as human milk (as is usually done, because casein in excess is not easily digested) the amount of butter is reduced to 12·7 per 1,000, instead of 43·43, which is the proportion in human milk. This is a shortage of approximately a teaspoonful of cream to every 4 oz. of the diluted cows' milk. If asses' milk, proportionately diluted, were used, the shortage of cream would be only half that amount. Now, amongst the poor one may say that cream is very rarely added to the milk prepared for babies' food ; only too often it is the other way and skimmed milk is given. Also the standard amount of cream in milk recognized by law is lower than that commonly present in good cow's milk, which still further enhances the evil. The common substitute of margarine for butter amongst the children of the poor is another factor which must not be lost sight of. Margarine is a mixture prepared from beef fat and vegetable oils, such as cotton-seed oil and cocoa-nut oil. It is extremely unlikely that any thyroid ingredient is present in this beef fat.

To sum up our conclusions then : Rickets is due to the lack of a thyroid ingredient which in the first months of life is obtained from the milk

of nursing mothers, the cream probably containing the chief portion of this ingredient. We may reasonably infer that a similar ingredient is contained in the milk of the cow and other animals, which may be successfully substituted for the mothers' natural milk if due regard be paid to the proportion of cream. Further, that cod liver oil is able in some measure to take the place of this ingredient, a fact which at least suggests the possibility of the iodine radical present both in cod liver oil and also in thyroid gland being the essential factor. Thus far we have looked on rickets as of maternal origin—that is, due to deprivation of thyroidal products, which would in the natural course of things be provided by the mother. It is at any rate evident that the thyroid gland of the newly-born animal is not capable of sufficient activity to save its possessor from rickets in the absence of any other source of supply, and it is also evident that if the thyroid gland of the infant be still unequal to its duties when the period of suckling is terminated, and sufficient subsidiary help be not forthcoming, rickets will still occur, though not in so severe a form as that arising at the earlier date. This is where the food factor is of so much importance. Milk with its cream as supplying the thyroid factor should still be a staple article of diet; but now the child should be able to digest

undiluted cow's milk, which will lessen the evil of fat deficiency, though the quantity will still be below the standard. Butter will also enter into the dietary, and, in the absence of thyroid depression from some debilitating influence, the child should now go on all right. It has become a much more general custom to boil milk nowadays for infant feeding. This is very good from the sterilization point of view, but there is no doubt that the milk is damaged in the process, partly of course by the injurious effect of heat upon the contained lecithin, and also because, as has recently been shown, cow's milk contains a very valuable ingredient in the form of lactalbumin which would probably be much damaged in boiling. The importance of lactalbumin consists in the fact that it is far more abundant in human milk than in that of the cow, and that it exerts a material influence in rendering the curds of human milk more flocculent and so more easily digestible than those of cow's milk. Possibly the thyroid ingredient of milk may also be damaged by boiling.

CHAPTER IV.

Fat and Thyroid Activity.

THERE is another factor which must not be lost sight of in the interpretation of the facts discussed in the last chapter, and that is the effect of fat on thyroid activity. The converse proposition has received considerable attention, and thyroid has been widely used as a fat reducer. It is, however, falling into disfavour, as experience shows that in many cases there occurs no reduction of fat appreciable from the cosmetic standpoint, so long as ordinary and safe doses of the drug are taken. The Editor of the *Medical Review* (October, 1910) points out that the effect of thyroid feeding is to dehydrate the fats of the body temporarily, the utmost results so obtainable occurring by the end of a week, but that excessive administration of thyroid may produce glycosuria, and there is already a latent tendency to glycosuria in many sufferers from obesity. I have administered 2½ gr. of thyroid three times a day for several months to a fat old woman with rheumatoid arthritis; the disease improved a great deal, but there was

no visible diminution in the fat. Nevertheless where increase of fat is accompanied by or due to thyroid deficiency, good results may sometimes be obtained, and have been reported from time to time, by thyroid medication.

I have such a case now under treatment. She is a woman of 32, and probably an example of the rare complaint described as "adiposis dolorosa." Her fat is massed particularly round the hips, and in this region she complained of pain, and was acutely sensitive to digital pressure. Her shins were also found to be very tender, which might suggest alcoholic neuritis. But this is not the case. She complained chiefly of pain over the sacrum and iliac crest, and of frequent and precipitate micturition. No other cause being found, she was put on thyroid treatment, which speedily relieved all her symptoms and decreased her weight by $9\frac{1}{4}$ lb. in six weeks. She still weighs 12st. $2\frac{1}{2}$lb., and tenderness can be elicited by pressure on the previously painful parts. Naturally she is continuing her treatment. Her diet has not been much altered, the chief item being the substitution of jam or marmalade for butter.

There are various points suggestive of some natural inter-dependence between fat and thyroid activity. Rickety children are commonly fat, as though Nature attempted in some

way to compensate for the lack of thyroid by the addition of fat. Contrast this fatness with the thinness of Graves's disease. Another point is suggested by the fact that two of the common symptoms of thyroid inadequacy are sensitiveness to cold and loss or scantiness of hair. In treating myxœdema, which represents, of course, total thyroid inactivity, great care has to be taken to protect the sufferers from cold. They are always worse if exposed to cold, and are often sent to warm climates on this account, though the thickened and sensitive skin seems to prevent them from having a subjective sensation of cold. Conversely the subjects of Graves's disease do not suffer from cold, but experience a constant and often unpleasant sensation of heat. Now, those races who are habitually exposed to great cold—the Esquimaux, for example—eat enormous quantities of fat, and the animals living in cold regions are provided by Nature not only with much fat, but also with most luxuriant hair or fur. Fur and fat are, of course, both bad conductors of heat, and so serve to protect their possessors from undue loss of heat. Doubtless the fat which is eaten helps by combustion to produce this heat. But it probably also assists by stimulating thyroid activity. We have already seen that thyroid deficiency is a factor in the production of baldness or loss of hair,

and naturally must assume that the converse holds good in some degree. The Esquimaux show further evidence of thyroid activity by being remarkably free from dental caries. There is, however, another factor, which would promote thyroid activity, and that is the iodine present in the fish food and possibly also in the fat of seals and other creatures which live upon fish. Possibly, we do not take enough notice of the natural likes and dislikes of people. Too often we are content to pass them over as idiosyncrasies without any inquiry as to whether they are not merely the outcome of some underlying law of Nature. But there is a natural instinct common to animals which tells them when to eat and when to abstain, and also what to eat and what to avoid. The same instinct is to be found in the human race, though unfortunately often dormant, stamped out by our vaunted superior knowledge, and various ideas often foolishly passed on from one generation to another. As a simple instance of the kind I mean is the craving for cold water experienced by many patients with fever. It is by far the most cooling and refreshing drink and provides the material for the beneficial sweating which is to follow, not to mention helping to flush the kidneys and wash away toxins and also correcting the tendency to constipation. But unfortunately

everyone except the patient has a horror of such a thing. It will give a chill, or upset the stomach, and so forth. Possibly if it has been long withheld artificially, the patient might take too much at first on having his wish granted. But had he been allowed to follow his instinct from the first, he would probably have gently sipped all he wanted, and been much more comfortable throughout the disease. I do not say that scientific reasoning is not superior to instinct, for it obviously is, but I do think there is often much to be learned from the natural instincts of the individual, if we only look for it. As another instance, A. Siegmund looks on distaste for meat as a certain sign of congenital or acquired thyroid deficiency. Apparently then "Jack Spratt's" wife who "could eat no lean" was the subject of thyroid deficiency. But it is equally evident that Jack Spratt, who could eat no fat, was the possessor of an active thyroid, and probably was constantly complaining that the fire was too big, and wanting the doors and windows open. He was not necessarily the victim of Graves's disease, though he might have been. These inferences can all be correctly made in the case of the four individuals who daily feed at my dinner-table, but of course it does not follow that there are no exceptions to the rule, and thyroid deficients will often be found who

do not like meat fat, but are extra fond of butter. The dislike of fat commonly shown by those who have active thyroids is open to two explanations. First, because of its heating propensities, secondly, because the thyroid secretion is antagonistic to that of the pancreas (W. Falta). It is therefore probable that antipathy to fat is sometimes caused by disability to digest it. The disability is an unconscious one, and in the presence of others enjoying the indigestible article the natural instinct may be obliterated, and the offence committed. Not infrequently the immediate result is vomiting. I recently came across a patient suffering from simple thyroid enlargement, who volunteered the statement that she habitually vomited "anything greasy." The vomiting had been an almost daily occurrence for a year, at the end of which time she had a very large goitre (girth 14½ ins.). When she came to me I prescribed thyroid, and the vomiting immediately ceased, while the goitre diminished. During the course of treatment however, shortly after a monthly period, her thyroid gland became larger and the vomiting returned. The vomiting was sudden, painless, and not preceded by nausea. It was again remedied by taking thyroid, and later when she left off medicine for a fortnight she vomited every day of the second week. Now the

evidence here is somewhat mixed. The simplest explanation is to leave the pancreas out of the question, and to say that the vomiting only occurred with those things which would ordinarily be likely to upset a sensitive stomach, namely, the "greasy" things; that the vomiting was analogous to the vomiting of pregnancy which has shown itself amenable to thyroid treatment, and commonly occurs in the early months of pregnancy, before the thyroid has had time to hypertrophy and assume the condition of hyper-activity normal to pregnancy. Why a pregnant woman should vomit in the absence of adequate thyroid secretion is another problem altogether. Is it due to toxins of fœtal or genital origin which are eliminated by an active thyroid? But this girl was not pregnant. She was, however, at an age of special uterine and ovarian development, a period which, as is commonly agreed, makes special demands on the thyroid. That the vomiting was due to thyroid insufficiency was proved by the fact that it was cured by thyroid and only recurred when she ceased to take thyroid and during a menstrual period when the supply of thyroid once more proved inadequate. The vomiting of pregnancy is not due to fats apparently, as in bad cases all foods alike are rejected. And it is not caused by thyroid inadequacy in itself (but by some factor

removable by thyroid efficiency), because vomiting is not a common accompaniment of thyroid inadequacy apart from pregnancy. Vomiting is, however, a common symptom of Graves's disease, and in some such cases, may well be co-related to the failure in digestion of fats owing to pancreatic insufficiency. W. Falta (quoted in *Medical Review*, November, 1910) states that thyroid hyper-activity diminishes pancreatic activity, and relates experiments showing that the inability to absorb fats depends on inhibition of the internal pancreatic secretion, not the external. Next arises the question, Is this pancreatic inhibition in Graves's disease beneficial and protective, or otherwise"? I cannot answer the question at present, for though the administration of "Holadin" (a preparation specially stated to contain all pancreatic extracts and ferment) speedily caused a complete alteration in the "fatty" appearance of the stools of my patient, in other respects she was perhaps not quite so well after taking this preparation for a fortnight. Now if we pursue these conclusions to a logical sequence, they are bound to influence our treatment of Graves's disease with at least some benefit. To reiterate briefly, I have endeavoured to show in this chapter and the last:

1. That milk, probably cream, and therefore presumably butter, contain an appreciable

quantity of thyroid substance, at any rate enough to save from rickets the infant whose own thyroid unaided is quite insufficient.

2. That probably fat has a stimulating effect on the thyroid.

I may now relate the results of treating Graves's disease on these lines so far as my limited observations have carried me. The subject of the following remarks had been treated for some fifteen months both by myself and others with varying success. She had just returned home from hospital after seventeen weeks in bed under open-air treatment and was certainly better, though far from well. She still had a pulse-rate of 120 or more, frequent palpitation, grossly exaggerated knee-jerks, tremors and a general sense of disability for exertion. On her return from the hospital I began treating her with thymus $2\frac{1}{2}$ gr. three times a day, and she continued to rest as previously. Both the patient and I thought she was improving slightly, though not a great deal. But one day after about a fortnight of this treatment she had some pork sausage for breakfast and within half an hour was taken with violent palpitation which lasted all day. I did not, however, see her until the evening, when she was rather better, but still very uncomfortable with a pulse-rate of 150 to the minute. The question arose, what could have

brought about this attack? Pork sausage, or bacon, or eggs for breakfast had on several occasions previously been responsible, but latterly she had been better and able to indulge with impunity. However, on going into the matter carefully it transpired that she had been having extra cream, milk and butter all the week, fish on two occasions, and chitterlings (pig's intestine) on the night before. She had not been conscious of any gastric disturbance and normally her appetite was healthy and bowels regular, generally twice a day. Her sister with whom she was staying, however, had received a present of some cream and bestowed the luxury on the invalid, which was so much appreciated that she subsequently had skimmed the household milk to obtain still further cream. Now the result is open to the interpretation that the attack was produced by giving these substances rich in products of thyroid activity to a patient who was already suffering from thyroidal excess. Some no doubt will say it was reflex—the result of gastric irritation from the sausage. Perhaps it was, but she had no gastric discomfort, furred tongue or any of the other symptoms that go by the name of "indigestion." So, acting on the first hypothesis, I put her on the very diet which would cause rickets in a child. I forbade cream, milk, butter or any

animal food whatever. She was to live for the time being entirely on vegetable food, largely farinaceous. I did not even at first allow lean meat. because although that did not save the young lions from rickets in the experiments already quoted, there is possibly a difference in the thyroidal ingredient, absent apparently from old horse-flesh, perhaps present in the meat of such younger animals as are killed for human food. I forbade eggs, because it is only logical to suppose that they represent in some way the thyroidal activity of the fowl. The yolk is the food specially designed for the young chick and is rich in fat and perhaps analogous to cream in thyroidal content. The patient had been taking thymus at the rate of $7\frac{1}{2}$ gr. a day for the fortnight preceding the bad attack, and this was at first continued during the period of abstinence from fat. The thymus appeared to be exerting a favourable influence on the symptoms, but as has been seen did not prevent the sudden and serious relapse. Now abstinence from fat appeared immediately to exert a more markedly beneficial influence than any treatment had done previously. The pulse in a few days dropped to 95 while the patient was up and dressed, though leading an invalid life. Previously 96 was the lowest that had been registered for months and that only during continued rest in bed. When

up the frequency was always 110 and often 120. She now improved at a more rapid rate than at any time previously during the illness. Within a fortnight she was able to take a walk of one and a half miles, more than she had done for fifteen months previously, and the day after her pulse was only 105. Further, the diet suited her general health and she gained 5½ lbs. weight in twenty-four days. The bowels were open two or three times a day but were not loose and there was no gastric disturbance. She then unfortunately took influenza in common with the other members of the household and naturally her condition did not improve. At the time of writing, however, she has stuck to her diet for two and a half months and thrives on it, though deprivation of butter appears to be a hardship. Olive oil takes the place of butter, dripping, or lard, in cooking. Later I found it necessary to allow lean meat as a relish for bread. The patient has improved greatly in her capacity for taking physical exercise and is able to carry out her domestic duties to a much greater extent than formerly, and can walk about two and a half miles without feeling any the worse for it. Nor has she had any recurrence of the bad attacks of palpitation. So far as it goes then the treatment is obviously beneficial, but it is equally obvious that one cannot expect to suppress

excessive thyroid activity by the mere removal of what may be regarded as thyroidal adjuvants. Another patient, who had been immensely benefited by ligature of her superior thyroid arteries on both sides some four years previously, reported immediate and considerable further improvement on abstaining from milk and butter. In this case, however, the patient, who weighed 10 st. $9\frac{3}{4}$ lb. in indoor clothes, lost 6 lb. in weight in a fortnight, and this may have caused the improvement, which consisted in lessened sense of fatigue with increased capacity for exertion. She lost 1 lb. more in the following month and maintained the improvement in health. The loss of weight was probably due to eating less bread, as jam, honey, &c., proved less palatable than butter. The pulse-rate was about 100 all the time, but the patient thought she was less nervous and obtained greater freedom from headaches. This patient's normal pulse-rate had been about 100 for some twelve months, but was subsequently reduced to 80 by a course of salicylates and cinchona, the influence of which drugs is discussed in a later chapter.

CHAPTER V.

Goitre—Calcium and the Thyroid Gland.

THE influence of calcium on thyroid activity naturally involves the consideration of goitre. Various views have been held as to the pathology of goitre. When I was a student I was taught that goitre was probably due to some germ flourishing in chalky districts. Accordingly, when I happened to live in such a district, I began making inquiries on my own account and questioned a good number of individuals suffering from goitre. I soon found that many of them never drank cold water at all. Whatever fluid they drank had been boiled and therefore sterilized, whether taken in the form of tea, or beer, or any other fluid commonly imbibed. Nevertheless, they still had goitres. Now calcium carbonate is, of course, precipitated by boiling, so it might be argued that the goitres were not due to excessive ingestion of calcium. This difficulty is, however, easily disposed of. Some of the calcium remains as "fur" on the inside of the kettle. But particles are so constantly rubbed

off that there is invariably a considerable quantity of calcium in suspension in the water, instead of being in solution. The stream of water from the tap, when the kettle is filled, is quite sufficient to loosen a large number of particles of "fur," and anyone who looks inside the kettle will see plenty of loose fragments, which have a happy knack of remaining in the kettle, clinging to the roughened inner surface, even when one endeavours to wash them out. The boiling of the water then agitates all these particles and, as I have often noticed, many find their way in powdered condition to the teapot, and in due course to the stomachs of the tea-drinkers. Calcium sulphate, if present, remains in solution. Similarly in cooking, calcium, though precipitated, may be served up intimately mixed with vegetables and other food. Thus, although boiling exerts a material influence on the amount of lime ingested, there still remains a quantity which may very well be the cause of goitre. I see no reason for supposing the presence of any rarer metal in combination with the calcium, though such may be the case. It is also more than likely that vegetables and fruit grown in a limestone district contain a higher percentage of calcium than those grown elsewhere. Also that the cattle living in such a district get more lime into their systems, both from grazing and

drinking hard water. If the cattle are possessed of active thyroids, they will assimilate lime to the full, and their milk will be rich in calcium. On the other hand, if their thyroid glands should be at all exhausted by dealing with so much calcium, the milk will be poorer in thyroidal substances. Thus, whether we eat meat or drink milk, or water, or consume vegetables, or fruit, in such a district our thyroid glands will be worked at higher pressure than if we lived in a soft-water district. The result will depend on how far an even balance be struck between thyroid capacity and the work required. If excess of work be demanded for a considerable time, it is only natural that hypertrophy should result. The commonest form of goitre is simple hypertrophy, and probably most, if not all, goitres start in this way. It may be objected that other glands in the body do not hypertrophy to any extent as the result of over-work, and why should the thyroid be an exception? But the case of thyroid hypertrophy is not quite on a parallel, as there is clearly some toxic agent at work. The spleen enlarges in typhoid fever, and to a much greater extent in malaria. Lymphatic glands enlarge in the neighbourhood of a septic wound. In these cases the toxin is clearly of microbic origin, though the actual irritant is presumably some chemical product of their activity.

In the case of goitre the irritant which causes enlargement is chemical, and I see no reason why it should be anything else than some form of calcium. But the precise method in which calcium acts needs elucidation. It is not difficult to explain the addition of an adenoma to the hypertrophy. It is supposed that adenomata are developed from small isolated portions of the gland called rests. These "rests," of course, get the benefit of the increased blood-supply, and are therefore extremely likely to share in the general hypertrophy. Other morbid changes doubtless occur as the result of irritation, inflammation, or degeneration. As to the manner in which calcium acts as a stimulant to thyroid activity, I think it is largely a question of antagonism, a dose of calcium calling for thyroid secretion in much the same way as a dose of carbonate of soda calls forth the acid secretion of the stomach. The analogy may be pressed further. If the dose of sodium bicarbonate be excessive, the stomach may not be able adequately to respond, and the contents may remain alkaline for some time, though in the absence of pathological conditions the acid-secreting cells soon gain the upper hand. So with the thyroid. Small doses of calcium use up the available secretion, and the natural result is that the thyroid sets to work to make more. If the dose be repeated

too frequently a period of exhaustion will follow. The exhaustion may be of short duration and the thyroid may quickly regain the upper hand. But if the exhaustion be prolonged, Nature sets to work to remedy the defect by installing more powerful machinery, in other words, enlarging the gland, or possibly organizing a system of continuous secretion, which, effectively done, would naturally produce Graves's disease. The fact of temporary exhaustion is, I think, well illustrated by Sir Almroth Wright's researches on the calcium content of blood in relation to coagulability. He found that calcium salts given for a few days increase the calcium coefficient and raise the coagulability of the blood. But if the dosage be continued the coagulability actually falls below normal. The most probable explanation of these phenomena would appear to be that the first doses of calcium stimulate thyroid activity, by which they are duly absorbed and received into the blood-stream. After a few days, however, the thyroid gland, owing to exhaustion or self-protective and inhibitory impulses, refuses to maintain work at this high level and is now unable even to absorb so much calcium as formerly from the food supply. Assuming excretion to continue at a uniform rate throughout, a shortage would thus soon occur, and this would obviously happen still

sooner if excretion occurred at a more rapid rate during the time of increased calcium intake. I had a patient in whom a few doses of calcium lactate so exhausted an already inefficient thyroid as actually to induce what I believe to have been a transient phase of myxœdema. The point is important, so I will quote the case more fully. Mrs. P., aged 37, had a goitre dating from puberty. It had increased in size with successive pregnancies, and became still worse after nursing her mother during a year's illness. She then went to a hospital, where the right lobe of the goitre was partially removed, but it appears that some difficulty arose, as the operation took four hours (this is the patient's story), and was not completed. She stated that on the whole she has been worse since. She had suffered much pain on the right side of the neck since, and had paralysis of the right vocal cord which made talking an effort. I mention this because it probably contributed towards depressing her general health. She still had considerable enlargement of the middle and left lobes of the goitre, causing dyspnœa, by tracheal pressure. Her neck measured $15\frac{3}{4}$ in. in circumference over the swelling, her pulse was 92 and her respirations 27. Bowels regular. No excessive thirst. Menstruation scanty as always, troublesome cough, great lassitude and

unfitness for exertion. She was corpulent and slept badly. Now in this case I confess I made a mistake. At first I thought that thyroid secretion was probably in excess rather than deficient. The evidence in favour of adequate secretion was the size of the gland, regularity of bowels, the fact that she was a mother, absence of menorrhagia, scanty loss of blood at confinements (indicating adequate clotting power of the blood), absence of thirst, and the somewhat rapid pulse. The pulse alone would suggest a leaning towards Graves's disease, but actually it was doubtless due to dyspnœa caused by pressure on the trachea.

Acting then on the supposition that my patient leaned towards Graves's disease, I first gave her arsenic and belladonna. She did not improve on this, so I thought I would see if some of this supposed excess of secretion could not be neutralized by calcium. Accordingly the belladonna and arsenic mixture was repeated and calcium lactate given in cachets of 10 gr. three times a day. She took four doses and next morning on waking found her face and eyelids very swollen, and not only her face but all her skin "felt very stiff and puffed." She did not take any more of the calcium lactate and the swelling improved the next day, but she did not altogether lose the sensation of stiffness in the skin for another two days.

There was no smarting or irritation, which negatives the explanation of urticaria. Equally certainly it was not due to the belladonna or arsenic, inasmuch as these were continued, and had also been taken for some days previously, without any such result. Unfortunately, I did not see her till the condition had practically subsided, and the explanation of myxœdema did not occur to me till several days afterwards. Then, however, I changed my tactics and gave her thyroid. The benefit was immediate and remarkable. There was a very obvious diminution in the growth, though the actual circumference only diminished $\frac{3}{8}$ in. during the six weeks she was under observation. It must be remembered, however, that the enlarged thyroid often spreads out to a considerable extent superficially, so that a single circumferential measurement of the neck does not adequately show alteration in size. Also the $\frac{3}{8}$ in. diminution on one side would represent $\frac{3}{4}$ in. difference had both lobes been present. Anyway, the patient felt very much better than she had done for years. She lost weight, and felt so well that she again left off her medicine, and only came back after a fortnight's abstinence from it to say how much better she felt, and to point to her decreasing size. Actually she was only 4 lb. lighter than she had been six weeks previously, but

the subjective sensation of well-being was very marked. If then calcium neutralizes thyroid secretion, it ought to be a useful remedy in Graves's disease. I think possibly it may be of some value, but there are obvious objections to its use. We have seen that it stimulates thyroid activity. This would be most objectionable in Graves's disease, and therefore the use of calcium would be limited to very severe phases in which one might fairly assume the thyroid was already doing its worst. I have used it under such circumstances and benefit has followed, but it is impossible to say without further experience whether it was due to the calcium or merely coincidence.

The hard-water districts of Kent, Surrey, Wiltshire and the Thames Valley, where ordinary goitre is prevalent, have produced a relatively large proportion of cases of the exophthalmic form (Ord and Mackenzie). It is, therefore, perhaps hardly rational to expect calcium to undo the mischief that calcium has done. On several occasions I administered calcium lactophosphate to a patient suffering from Graves's disease in a comparatively mild form, and it invariably made her worse, presumably because her thyroid was still capable of further stimulation. Later I tried the effect of limewater, 1 oz. three or four times a day. This did not produce any immediate

result that I could detect, but later I came to the conclusion that it did harm rather than good. The pulse-rate was a little quicker and the blood-pressure undoubtedly considerably higher. This fact alone is a good reason for not giving calcium, unless it can be shown that the gain is greater than the loss. If the blood-pressure be raised and the pulse-rate do not decrease in frequency, the heart is obviously burdened with increased work, a result distinctly to be avoided in Graves's disease. Moreover, the patient complained of an increased sensation of hissing in the ears with each heart-beat, which one would think was probably due to the blood being forced through the carotids at this increased pressure. If calcium is to be given in Graves's disease it would appear that the best mode of administration would be occasional large doses for not more than one or two days in succession, repeating the dosage after a week's interval, if indicated.

Thus far, we have considered calcium chiefly from the point of view that in excess it does harm, and probably in all cases of simple goitre it would be well to eliminate calcium as far as possible from the dietary, and to avoid it altogether medicinally. But there remains a large group of cases (non-goitrous) in which calcium is useful, especially if given with thyroid. This includes many of the cases of thyroid

insufficiency, where stimulation is distinctly useful. But even in these cases a little discretion is necessary. If the gland be fatigued as the result of overwork, it is obviously better to rest it, rather than exhaust its remaining activity with a drug like calcium. Therefore, in many cases, it will be well to commence treatment with thyroid alone, or possibly, combined with small doses of some preparation of iodine (syrupus ferri iodidi in five-minim doses answers admirably), and when the gland has had a few weeks of such assistance, a little calcium will be beneficial. I find the syrupus calcii lactophos. a most useful preparation in such cases, and am inclined to think the phosphorus element is also beneficial in stimulating the thyroid. It has given me good results in thyroid inadequacy, and seemed to be less tolerated in Graves's disease than other preparations, but there may have been some other factor at work. Calcium is obviously called for in conjunction with thyroid, in all those diseases in which there is apparently a deficiency of calcium in the blood or tissues. This probably includes all hæmorrhagic conditions, in which we must not forget to include a special liability to bruising from trifling injuries, various forms of purpura and also chilblains. The latter are quickly benefited by calcium salts alone in most persons, but probably the calcium ingested with the food would

be sufficient if thyroid activity were up to the mark. Many forms of urticaria are benefited by calcium, and thyroid has also proved of very great assistance, often proving effective without any calcium other than that in the normal food supply.

At the same time it must be noted that urticaria sometimes appears to be the result of thyroid excess, and I have seen it produced by continuous or large doses of thyroid substance. This anomaly requires further elucidation, but it almost looks as though calcium metabolism may, under such circumstances, proceed so rapidly that excretion exceeds absorption, and so a deficiency occurs. This supposition would also explain the occasional presence of chilblains in Graves's disease.

It has only fallen to my lot to treat two cases of giant urticaria, a condition which some would term angioneuritic œdema. Itching, so far as I recollect, was not a prominent symptom in the first case, but it certainly was intense in the second. Otherwise both cases were very similar, large patches appearing on any part of the body, including the lips, eyes and face, with the result that the aspect of the patient was altered beyond recognition. The first patient also had the mucous membrane of her mouth and throat affected, causing such urgent dyspnœa as to make one wonder whether tracheotomy would be required. The affection

in any particular place did not last more than about twenty-four hours in this patient, but the liability to it did not show any very rapid improvement under the continued administration of calcium lactate, though ultimately the girl got well. My second case was a girl of about 20, and from the first I administered thyroid with calcium lactate. She improved much more rapidly than the other, her urticarial patches only lasting a few hours, and ceasing to appear at all after about three weeks' treatment. Previously she had suffered intermittently, but frequently, for about two months, and she showed other signs of thyroid inadequacy, which improved concurrently under treatment. There has been no recurrence for over six months at the time of writing.

There are, of course, many agents which will produce urticaria, and it is difficult to suppose that the thyroid and calcium supply are always affected. Some suffer within a very short space of time after eating strawberries, and others after eggs, even the small amount of egg in a single piece of cake being ample to produce an attack. It is, nevertheless, a tempting supposition that different individuals manufacture different toxins and that the thyroid, if efficient, ought to be able to deal with any toxin unless in overwhelming doses. The condition of each individual thyroid doubtless varies frequently, according to work performed, and so may be

unable at one time to deal with a toxin that would be efficiently neutralized at another. I have many times been stung by bees, but only on two occasions did this produce urticaria. It does not seem highly probable that the formic acid injected by the bee varies very much in quality, so the explanation must be looked for in my own condition, though I doubt whether I had much more than heard of the thyroid gland at the time. On the first of these occasions, I had five or six stings on my hands, owing to my foolishness in handling the bees with woollen gloves on. The bees get their legs entangled in the glove, and vent their wrath immediately. Within half an hour I had an intense urticaria over my whole body from feet to face, accompanied by intense headache and intolerable itching, which lasted about two hours. On the second occasion, after one sting on a finger of the right hand, the urticaria, which was much admired by a medical friend, was limited to the right arm and fore-arm. As I have said, stings on other occasions never affected me except locally, so the urticaria might have resulted during a period of lessened thyroid activity or calcium deficiency. At any rate, there would be no harm in giving calcium and thyroid treatment a trial, in most cases of urticaria, not forgetting the elimination of any offending toxin, where there is any evidence of such a factor being present.

CHAPTER VI.

Goitre—Iodine and the Thyroid Gland.

One cannot always tell at the first glance whether the secretion from an enlarged thyroid is adequate for the needs of the body or excessive. The fact of enlargement points to a previous demand for secretion, and an attempted response on the part of the organism. The response may be insufficient, adequate or excessive, and the conditions will naturally vary, being further influenced by possible changes in the requirements of the organism. But speaking in general terms, the patient with an enlarged thyroid probably has more secretion than one without. Many patients with enlarged thyroids are practically free from the stigmata of insufficiency, though signs and symptoms of previous insufficiency can often, indeed usually, be found. And in not a few cases secretion will apparently be slightly excessive. This is merely the result of a natural sequence of events. There is a period of thyroid exhaustion followed by compensatory enlargement and increased secretion. If the secretion become excessive, a reflex diminution

of the gland is likely to occur, and the goitre get well. This sequence is constantly seen in the goitres of puberty, many of which get well spontaneously, the cure being attributed, in many cases, to any cause but the right one. But cure does not always follow. Some pathological factor steps in and interferes with the natural sequence. Here is our opportunity for investigation. The case must be gone into thoroughly, and by careful weighing of the various details there is reasonable chance of arriving at a satisfactory conclusion. Elimination of unfavourable influences will materially improve our success in treatment. Unfortunately, the difficulty is to know what are the unfavourable influences. The possibility of pulmonary tubercle must always be remembered, and if present this must have the prior claim to treatment. Constipation must also be reckoned as one of the unfavourable influences, and I have noticed an immediate and marked diminution in the size of a goitre produced by attention to this simple point. I had been administering thyroid to this patient for a month without success, and purposely did not give aperients, because I hoped to witness the beneficial effect of thyroid in this direction. It became evident, however, that purgation was a necessity, and the immediate result (within four days) was a diminution of over an inch in circumference of the

goitre, with marked softening and shrinking of the growth. I have already remarked that a single circumferential measurement of a goitre is a fallacious method of estimation. The reason is, that in many of the largest goitres the greatest measurement is a little below the cricoid cartilage. One naturally measures the greatest circumference, which is usually obvious. When the goitre begins to diminish there is a vertical shrinkage, and often a very obvious diminution in the upper poles of the gland. The maximum girth will now be found rather lower down than previously, and a measurement taken here obviously does not give a correct impression of the difference in the size of the goitre, as the neck itself (considered apart from the goitre) has an increasing circumference towards the lower part. The circumference may also vary with the position of the neck, to the extent of over half an inch. Some patients are able to get the sterno-mastoid muscles forward, over the lateral margins of the goitre and so compress it, more or less like a sponge. This diminishes the appearance of the goitre even more than it does the actual measurement, but naturally applies especially to the softer varieties. Sometimes variations in size are transitory and of purely vascular origin, and I have observed a goitre enlarge during palpation. This patient said the swell-

ing always got larger when she was excited or flurried. Enlargement commonly occurs at each menstrual period, which argues that some internal secretion of sexual origin has an antagonistic and therefore stimulating or exhausting action on thyroid secretion.

Goitres also occur at the menopause, and thyroid gland has been administered with some success in the "flushings" so prone to occur at this time of life. The *rationale* is not very clear. The menopause is probably a period of paroxysmal ovarian activity. It has always appeared to me that "flushings" are due to paroxysmal thyroid activity. The one may depend on the other, or both may be merely, so to speak, the dying convulsions of glands which are doomed to relinquish their most important functions.

Undoubtedly some cases are benefited by administration of thyroid, and others, of ovarian substance, but I have not yet learned to discriminate between these two. "Flushings" may occur after double ovariotomy, and therefore may well depend on thyroid activity independently of ovarian stimulation or antagonism. They may of course be due to loss of ovarian antagonism—a spasmodic overflow of thyroid secretion not neutralized by secretion of the ovaries, on account of waning function in the latter. On the other hand, I found that men-

struation was induced, after periods of amenorrhœa lasting nine and ten months, in a patient who had been subjected to double ovariotomy a little over two years previously. This patient had suffered from life-long constipation, and showed other signs of thyroid deficiency. Thyroid medication was decidedly beneficial, but in about seven weeks menstruation occurred and was repeated four times at intervals of about a month during the time the thyroid was being taken. This is evidence that the thyroid influences uterine activity apart from ovarian secretion, and therefore it is possible that the converse is true also.

The case is, however, open to a different interpretation, and may be merely another illustration of the necessity of thyroid for calcium metabolism. Recent research has shown that menstruation itself is dependent on calcium metabolism, that calcium is in some cases a remedy for amenorrhœa, and is actually excreted during menstruation. The natural tendency is for the calcium co-efficient to rise before menstruation and fall after, and irregularities in this process may be responsible for many of the ills to which the female flesh is heir. It is an interesting fact that the headache from which so many women suffer, especially after the period is over, may be benefited, or eliminated, by the administration of calcium. In

the case under consideration, it is possible that administration of thyroid merely caused increased assimilation of calcium from the food supply, and so, indirectly, induced menstruation.

The activity or otherwise of an enlarged thyroid is also very important from the surgical point of view. When one half, or even the middle lobe only, of a parenchymatous goitre is removed surgically, it is usual for the remainder of the growth to disappear rapidly and spontaneously. One of the great dangers of the operation is death from acute thyroidism. So much thyroid secretion is turned loose into the system by the necessary manipulations and by leakage, not only during, but after the operation, that the patient commonly shows signs of thyroid intoxication, and a good many deaths have occurred. But is not the big dose of thyroid secretion thus absorbed the immediate cause of the atrophy which follows in the favourable cases? The nervous system flooded with thyroid secretion sends powerful inhibitory messages to the gland, which accordingly atrophies to a reasonable size. But I have already quoted one case, in which part of the gland had been removed, and atrophy of the remainder did not occur. And in this case it was shown by subsequent events that the thyroid gland was peculiarly impotent. Hence, the patient's system did not get flooded

with secretion at the time of the operation, and the favourable termination did not result, though an extraneous supply of thyroid immediately proved beneficial.

Cases have been recorded to show that removal of the middle lobe only (a comparatively simple and far less risky operation) is sufficient to cause atrophy of the rest of the gland. This result cannot be a question of blood supply on anatomical grounds, and certainly favours the explanation already given. But what we usually have to fear after an extensive operation is thyroid toxæmia. Recently I assisted at the removal of one half of a very large thyroid which was obviously secreting too much for the welfare of the patient. We feared the case might drift on into well-marked Graves's disease. Immediately prior to the operation the anæsthetist had administered a hypodermic injection of strychnine and atropine, which I believe proved highly beneficial. The patient was remarkably free from thyroidism after the operation, and I suggest that the atropine was responsible, inhibiting secretion during the operation, and for some hours after, and thus reducing the dangers of toxæmia. Nevertheless, atrophy of the remaining lobes occurred within a few weeks, so the dose of thyroid secretion administered by surgical interference was still adequate, though not

dangerously excessive. Some have suggested that goitres are of an inflammatory nature. This is possible, some being distinctly tender, but the outward and visible signs of inflammation are often conspicuous by their absence. It may be argued that the secretion from an enlarged thyroid is ineffective, because the percentage of iodine in the colloid of such a gland is usually found to be below the normal. This may be a correct conclusion, but is not necessarily so. By enlargement, the amount of available secretion is increased, and if the actual amount of iodine remained the same, or even slightly increased, the percentage would nevertheless be lower.

But a deficit of iodine may obviously result either by excessive use, or shortage of supply. The question of supply, taken all round, is probably not a very variable one, and is at least unlikely to account for a goitre in one member of a family, whilst the others who feed at the same table escape. It would be a useful piece of research work to ascertain what substances commonly eaten contain iodine, and in what proportions. Sea-weed, which is used as a commercial source of supply (or at any rate was so used before the American saltpetre was found to contain iodine and to be more profitable to work), only contains ·5 per cent. of iodine. But iodine is probably present in

many vegetables and fruits, though in much smaller quantities. Also in fish, seeing that the food of the latter is derived primarily from the sea-weed which is eaten by various molluscs and animalculæ, which in turn are eaten by the fish. But a shortage of iodine affects whole districts, as related by Dr. A. Rendle Short in the *Bristol Medico-Chirurgical Journal* for June, 1910. In certain North American districts remote from the sea, serious loss occurred from the number of cretin lambs. Many of the sheep and dogs were goitrous. But the introduction of an iodiferous salt, in place of pure rock salt which had previously been administered to the creatures, proved an effective remedy. But shortage of iodine is much more likely to occur as the result of excessive use, rather than deficient supply. The causes of such excessive use, in other words, the causes of excessive output of thyro-iodine, and resulting thyroid exhaustion, are still somewhat obscure. We have already made mention of the influence of ovarian, and possibly uterine activity at puberty, in childbearing, and at the menopause. Also of the influence of lactation, and of various diseases which induce thyroid exhaustion. Goitres may also occur in the male sex at puberty. There is obviously no reason why a goitre should occur as the result of brief temporary thyroid exhaustion. But

several months of pregnancy are sufficient to produce a palpable enlargement of the gland, perhaps hardly deserving the opprobrium of the word goitre. Any condition which makes a sufficiently prolonged demand on thyroid activity will tend to produce hypertrophy, or goitre. But the greater the natural activity of the gland, the less will be the need for hypertrophy. Therefore when goitre occurs, it is either a confession of inadequacy, or a protest against excessive dissipation of thyroidal products. This dissipation may be apparently brought about by drinking water to be found in certain limestone districts, where, as a result, goitre is prevalent. I explain this on the simple assumption that all calcium entering the system is immediately, as it were, ushered in to the thyroid gland department. Thence, it is duly distributed to all the calcium-requiring tissues in the body, any surplus being only excreted as waste. Precisely how this distribution occurs is for me merely conjecture. But as a very crude suggestion let us suppose for a moment that in the process of absorption, all calcium has to be turned temporarily into calcium iodide, the iodine being afterwards again liberated into the blood stream, and so sent back to the thyroid as a "returned empty." One can hardly suppose the process to be so perfect that there is no loss. Some of the

"empties" are never returned at all. But with reservations, the more calcium ingested, the greater the loss of iodine from the thyroid gland. The ultimate result, however, depends on *other* factors. Not all the people in the district get goitres. So those who escape presumably are possessed of more capable thyroids or are less subjected to demands in other directions for thyroid secretion, or possibly in virtue of idiosyncrasies as to diet get more iodine into their systems. The amount of iodine required is of course exceedingly small. The marvel is, that an element present in the system in such minute quantities should be possessed of such profound potentialities. "Behold, how great a matter a little fire kindleth." The development of goitre, however, does not in any way remedy the iodine deficiency unless an enlarged thyroid contains more iodine than a small one. Dr. Rendle Short suggests that the thyroid enlarges in order "to catch more iodine from the blood stream." But possibly a small thyroid could catch all the iodine normally present, and it seems more probable that hypertrophy is merely the result of increased blood supply induced by increased secretion. If iodine material is wanted in the body there occurs a reflex activity of the thyroid gland. If the resulting secretion, on account of deficiency in

iodine, does not satisfy the needs of the body the demand for more secretion is still insistent and increased blood supply becomes continuous, resulting in over-nutrition and hypertrophy. When once hypertrophy is established it takes a considerable time to reduce the thyroid to normal dimensions. And though in the case of the sheep already mentioned, an adequate supply of iodides could prevent the occurrence of goitre, the cure of a goitre once established is a different matter. Many goitres are never cured by iodides at all. Those that are generally take a long time. This may be because we do not at present know how to present the iodine in a form ready for immediate use. Iodide of potassium, for instance, is quickly eliminated in the urine. The exact proportion so recoverable I do not know. Thyroid gland substance or thyro-iodine itself would naturally give the best results, but even they hardly come up to expectations in rapidity of action. Even supposing that we provide the patient with sufficient thyro-iodine to render the thyroid potentially idle, the question of atrophy is not fully solved. If an athlete lie in bed his muscles will certainly waste and get flabby, but (apart from debilitating conditions), the muscles, even after some weeks, may still be bigger than those of a non-athletic man. There is naturally another factor to be

considered, namely, where and why the iodine wastage occurs. Goitre is but a symptom and Science must find and treat the cause. The cause is often, if not always, complex and may involve factors which are still operative as well as those which have passed. And in looking for the causes one must remember all those which we have seen to be productive of thyroid deficiency, inasmuch as goitre is a product of continued thyroid deficiency in special individuals under special conditions. The logical sequence of these conclusions is that thyroidectomy (though possibly necessary in some cases) is not the scientific treatment of goitre. The result may appear to be perfectly successful at the time, as indeed it did in the case of the patient last quoted. The goitre, as mentioned, *entirely* disappeared, and she felt better than for years previously. But six months after her operation she again noticed some enlargement of the remaining lobe, and four months later still there was a very obvious enlargement, thus proving that the demand of the organism for thyroid secretion was still insistent, and Nature was again attempting to supply the want by inducing hypertrophy of the remaining portion of the gland. We therefore yet need to be shown a more excellent way, for thyroid medication does not always solve the problem.

CHAPTER VII.

Iodine and Graves's Disease.

THE victim of Graves's disease usually develops a goitre. In some cases the order may be reversed, and the victim of a goitre may develop Graves's disease, but not infrequently the first condition is one of hyperactivity in a normal sized thyroid, and the goitre develops as the result of such activity and increases in size as the disease progresses. But here the products of secretion are in excess of the demands, and so far as we can see, exert only a baleful influence. Many of the symptoms of Graves's disease, as pointed out by Rendle Short, are similar to those occurring in iodoform poisoning, from which he argues that iodoform poisoning is a condition of acute thyroidism. He cites the authority of Oswald, Hunt and Seidell that iodides and iodoform increase the amount of iodine in the thyroid colloid, with a corresponding increase in its physiological activity. But one must not lose sight of the fact that in iodoform poisoning the iodine is introduced from an

extraneous source in relatively large quantities, and though it may stimulate thyroid activity to excess, some of the iodine probably enters the system regardless of the thyroid, or filters through it, producing results the same as those of over-production. To look at the matter in a slightly different light, Graves's disease may be considered as a form of chronic iodine poisoning, though we cannot suppose that there is usually any continuous or excessive supply of iodine from extraneous sources. Whence could it come? The victims of Graves's disease are commonly eating the same food and are subject to the same influences as other members of the household who do not so suffer. If, then, the symptoms of Graves's disease are not due to excessive intake of iodine into the system, may they be due to diminished loss? This position seems hardly more tenable than the other. At the same time we should be glad to know how iodine is normally excreted from the system, for though iodides medicinally administered may be quickly detected both in saliva and urine, I have never been taught that iodine is a normal constituent of urine. Dr. Rendle Short suggests as a remedy for Graves's disease an iodine-free diet. This is difficult to accomplish because the normal intake is so small that we hardly know whence we do get it. But the potency of

a minute quantity of iodine, in a really assimilable form, has already been shown in the absence of rickets from babies and young animals at the breast. It follows that an iodine-free diet involves abstinence from milk and cream, and probably also from butter.

When looking for a substitute for butter to carry out this plan, a patient lighted on a preparation called walnut butter, which was not unpalatable or expensive. But I was informed that analysis showed a considerable quantity of iodine. This merely illustrates the difficulty of arriving at an iodine-free diet. Dr. Rendle Short suggests lean meat for this purpose. But several authorities state that raw meat is an excitant of thyroid activity. (Dr. Arnold Lorand quotes three authorities in an article published in the *Lancet*, November 9, 1907.) I do not know to what extent cooked meat possesses the same properties. Leonard Williams states that "meat-food, and alcoholic drinks in excess, are depressors of thyroid activity." The only way to reconcile these two apparently contradictory statements is to say that meat stimulates, and therefore, in excess, exhausts thyroid activity. Leonard Williams writes with special reference to cases of thyroid inadequacy, and these would naturally show exhaustion readily. If, then, we adopt the meat diet for Graves's disease, we have to

run the risk of possible thyroid stimulation. Dr. Chalmers Watson produced goitre in fowls by limiting them to meat diet. Dr. Rendle Short's explanation of this, is that goitre was due to iodine deprivation, as in the case of the North American lambs. I am not prepared to decide which of these three views may be the correct one, but, indirectly, all are possibly true. It is a significant fact that thyroid deficients have an instinctive dislike of meat. And lean meat proved useless in the prevention of rickets when given to the lion cubs at the "Zoo." If it stimulated the thyroids of the young lions, there was evidently no response, perhaps owing to the absence of a working supply of iodine. But even if we succeed in evolving an iodine-free diet, we do not really strike at the root of the trouble, inasmuch as Graves's disease is only exceptionally due to an excessive supply of iodine (*i.e.*, in those cases induced by iodoform poisoning). The same objection applies to the alternative of finding some means of eliminating all the iodine from the system, by means of the water of a goitre well. Nevertheless, if we could by these means obtain control of the iodine factor, we might hope so to arrange matters that the thyroid might be induced to return to its former state of responsibility in regulating the metabolism of this essential element, without

"running amok," as it does in Graves's disease. But I do not think the cause of Graves's disease is to be found in a simple accumulation of iodine. I humbly offer the following theory of its pathology. I suggest that the thyroid glands of all of us normally contain a certain amount of iodine stored as an inert compound, a gradual disintegration taking place, according to the dictates of the animal economy. This supposition has many physiological parallels in fibrinogen, mucinogen, glycogen, and all the other "'gens" or substances by means of which a material is stored inert until required. Now we know that the amount actually present, though not great, is fairly constant in health; that the intake is necessarily variable and precarious, and the normal excretion is so small that, so far, we are hardly able to do more than conjecture about it. It is only natural, then, that some provision should be made for the preservation and retention in the body of such an essential material, the supply of which is so precarious. In short, that the same iodine is used over and over again, being liberated from the thyroid storehouse, performing its functions, (one of which, is that of acting as a lime-carrier), and returning empty to the thyroid, where it again enters into suitable combination and is again stored till required. Under these conditions it seems probable that Graves's

disease is the result of an excessive discharge of the reserve iodine into the system, by the chemical disorganization of the substance which normally holds it in storage. The iodine thus turned loose into the system produces the well-known group of symptoms collectively known as Graves's disease (many of which, as we have seen, are present in iodoform poisoning); and is re-collected by the normal conservative system, returned to the thyroid gland, and again discharged before it is required, so keeping up the condition of toxæmia. Thus a sudden explosion in the iodine stores of the thyroid gland is all that is needed to flood the system with iodine and start Graves's disease. This is probably what occurs when the disease is started by a fright, or a sudden shock, a mode of onset which suggests that the exploding spark may be some product of nervous katabolism. The well-known nervous symptoms of the disease further suggest that perhaps such a product is being continually formed, and exploding the iodine storage material as fast as it is re-formed. I do not wish to lay undue stress on this suggestion as to what the exploding agent may be. For we do not know by what agency iodine is normally set free from the thyroid gland, though we suppose that it is governed by laws of chemistry, controlled by nervous impulses. A sudden

shock sends impulses helter-skelter down any of the nerves, and may produce various physiological results—a leap, a shout, the secretion of tears, vomiting, or the passage of urine. Why not also a thyroid explosion? It is not so easy to explain why the condition should become continuous in the case of the thyroid, though transitory in the instances quoted. But permanent disorder of the brain may follow sudden shock. Why not long continued or permanent disorder of the thyroid innervation? Again, destruction is always more rapid than construction, and it may well take a long time to capture and firmly tie up this iodine which has got loose in the system. Possibly, a "vicious circle" has become established.

In those cases where Graves's disease becomes grafted on to an ordinary parenchymatous goitre, perhaps one may suppose that the gland, in response to the needs of the organism, has acquired a habit of throwing all available iodine into the circulation. But when the iodine is no longer required in quantity, owing to alteration of the conditions which previously demanded it, the inhibitory mechanism having lain idle for some time has got rusty and will not work. A habit has been formed which is hard to break. Such a condition is comparable to the repeated discharge

of nervous energy in epilepsy, or perhaps to the continued transformation of glycogen into sugar in diabetes.

Next let us consider how far the surgical treatment of Graves's disease bears out or contradicts these theories. Briefly, the surgical treatment consists in removal of part of the gland or in cutting off part of the blood supply. It is evident in the former case that the removal of part of the gland, with any iodine material it may contain, will do good if the symptoms of Graves's disease are due to iodine toxæmia. Further, part of the iodine storehouse is removed, and therefore however inefficiently the regulations for supply and demand may be working, the thyroid is now incapable of flooding the system to the same extent as formerly. Ligature of blood vessels to the gland produces similar results by a process of atrophy. It would, therefore, appear that one cannot expect surgical treatment, *ipso facto*, to cure the disease. The symptoms certainly will be improved, but the resulting condition will depend on how far an equilibrium has been restored between supply and demand. If the remaining portion of gland be still sufficient to contain more iodine than is required by the system at any given moment, and owing to faulty innervation the whole or greater part of that excessive quantity be poured into the

system, a condition of Graves's disease will still remain, though obviously the toxæmia will be less. Cure will only result by an adjustment of the nervous control, failure of which has given rise to the disease. This adjustment is naturally more likely to be brought about if we can improve the bodily health. So it is still right to attack the various symptoms if by so doing we improve the general condition, though obviously we should strive to turn the stream of evil as near the source as possible. We must try to solve the various problems which appear to be presented. What causes this constant explosion of the iodine material? What is the normal agent which sets free thyro-iodine from the gland? Analogy suggests that it is some ferment. The symptoms of the disease and its common mode of origin suggest that it is some product of nervous katabolism. But possibly the thyroid is trying to accomplish some good purpose in this excessive secretion. Perhaps the sufferer from Graves's disease is thus saved from some other condition which might be even worse. Obviously the mere attempt to neutralize thyroid secretion, or to exhaust the thyroid gland, is not the most scientific procedure. Any attempt to neutralize the secretion, if successful, would tend to stimulate the production of more. But till we have solved these problems,

we may very well try to obtain some control over the iodine supply and demand. This involves a study of all those conditions which have any bearing on thyroid activity. The plan which commends itself to me, is to put the patient on a diet which has been found by experience to be conducive to rickets, which I have already gone into. I have not yet completed my tests of this treatment, but the immediate results in two cases have been very encouraging. It is unsafe to argue from solitary cases, as individual idiosyncrasies and coincidences, depending perhaps on other unobserved factors, may lead one to hopelessly wrong conclusions. I do not wish in any way to discount the recognized methods of treatment of Graves's disease by rest in bed, open-air, electricity, the application of ice to the neck or præcordium, inunction of the gland with red iodide of mercury, the administration of thymus, "rodagen" and other "anti-thyroid" bodies, nor the use of such drugs as phosphate ofsoda, arsenic, belladonna, digitalis, and so forth. Those who study the matter will be able to form their own conclusions, and it is well to have a method in one's madness. Successful cases have been published from time to time treated by widely different methods. One of the difficulties in estimating results is, of course, the tendency to a spon-

taneous cure, after a variable period, in most cases. The last used treatment is likely to get the credit, and very likely be published if the case has been a long one, inasmuch as other recognized methods, perhaps in skilful hands, had previously failed. It is a trite saying that the longer the list of remedies for any disease the more futile they are likely to prove. A remedy which has proved useful in the hands of one may appear valueless to another. Take for instance digitalis. I believe that most observers are agreed that it is of little value in Graves's disease. If it does not slow the pulse, it probably does raise the blood pressure, which is theoretically wrong. Yet such an observer as Trousseau was a strong advocate for digitalis. Possibly he may have been the possessor of a potent form of digitalis, which appears to vary greatly according to the soil and climate. Personally, I have given up using non-standardized preparations of the drug, and generally rely on Nativelles' granules of crystallized digitalin, if an immediate and certain result is necessary. One patient whose case has already been discussed was also very definite in her reliance on these "little pills" as a remedy for palpitation, though she did not know what they were.

I cannot help thinking that the administration of thyroid in Graves's disease deserves

more consideration than is now commonly accorded to it. In the early days of thyroid knowledge it was doubtless frequently given, and probably in very excessive doses. In most cases, it not all, one must assume that large doses would be badly borne. But some successes have been reported. Are these all to be regarded as coincidences? The argument against thyroid is patent to everyone. When the gland is already secreting a lot too much, why give more? But there is another equally cogent argument on the other side, though not quite such a superficial one. May we not suppose that in Graves's disease there is some other primary condition at fault, a toxin or what not, which the thyroid gland is heroically endeavouring to counteract. But like some other well-meant endeavours, it does more harm than good. In other words the remedy is worse than the disease. Now if this be a correct view of Graves's disease, it is obvious that a small dose of thyroid, several times a day, may very well intercept or restrain this insistent demand for the secretion of the patient's own gland. By continuance of such treatment, one might hope to dull the nervous susceptibilities of the gland to the constant demands made upon it, and by degrees to lessen the habit of hyper-activity. The addition of further thyroid might even accomplish

the task which the gland is attempting to perform, thus removing the source of the evil. The same arguments are of course applicable to large doses of thyroid, but one can readily see that the immediate effect would be to increase the evils of hypersecretion, and possibly the patient might succumb. Anyone using large doses would therefore in all probability speedily be forced to desist. This line of treatment would therefore have to be used only in the earlier cases, and they would need to be put to bed for the purpose.

CHAPTER VIII.

Lymphatic Glands and Graves's Disease.

In the last chapter some stress was laid on the possibility of Graves's disease being the result of an explosion in the iodine stores of the thyroid gland, and consequent poisoning of the system with iodine in the highly toxic combination, in which it is normally supplied to the tissues by the thyroid gland. It was suggested that the explosion may occur as the result of a fright, or of prolonged nervous stress. A "nervous" condition is sometimes the precursor and apparently the cause of Graves's disease. On the other hand, Graves's disease certainly highly increases any nervous symptoms which were previously existent, and originates others. Here is possibly the vicious circle which makes Graves's disease so hard to cure. But there is no reason why the disease should not be started in other ways. I have already suggested diabetes as a parallel. Numerous and varied are the causes which appear to be factors in the production of diabetes. Yet when the disease is established the whole group of symptoms is sufficiently

characteristic to be designated by a definite name, though obviously if one can differentiate the mode of origin, a definite line of individual treatment is more likely to be successful than the usual general measures. Similarly in Graves's disease we have a general grouping of symptoms sufficient to mark the name of the ailment, yet varying in different individuals to a considerable extent, and possibly, as in diabetes, there are various modes of origin. Any cause which evokes thyroid secretion may, theoretically, be a cause of Graves's disease. The question is practically one of supply and demand. There is in Graves's disease a curious association of several factors, a manifestation of activity in other glands. The thymus is said to be invariably enlarged, and usually one finds enlarged lymphatic glands in the neck. This latter symptom is all the more curious because, as Leonard Williams remarks (and I have often been able to confirm it), children who are thyroid deficients, very frequently have enlarged cervical glands, and the administration of thyroid extract causes atrophy of these compensatory hypertrophies. Conversely, however, the administration of thyroid substance is said sometimes to cause enlargement of the glands under the angle of the jaw, which hypertrophy disappears when the remedy is left off. In this latter

case, however, there is perhaps the question of tubercle, which seems to thrive on thyroid medication. The glands under the jaw, and therefore nearest the tonsils, would probably form the first line of defence. Probably in all of us these glands are dealing with tubercle bacilli pretty frequently, fortunately with success in most of us, and it is possible that thyroid medication assists the tubercle bacilli to the extent of necessitating glandular enlargement, though no further mischief appears to result. The same explanation would of course be applicable in Graves's disease, the enlargement spreading to most of the cervical lymphatics under the influence of prolonged thyroid activity. But this explanation does not seem highly probable in either case. If it were so, we should almost certainly meet with caseation and suppuration in such tuberculous glands not infrequently in cases of Graves's disease. Yet such an occurrence must be rare. Therefore we must look for some other explanation than tubercle to account for these enlarged cervical glands. It is probable that the morbid condition which stimulates thyroidal activity is so urgent, that it affects what may be called the deputy-thyroid organization as well. The age for gross enlargement of tonsils and adenoids is now passed, so they are not added to the picture. In

lymphadenoma hypertrophy of adenoid tissue in the pharynx as well as other parts is commonly present. In this disease also the first glands to enlarge are commonly these same cervical glands which we have just been discussing. Further, in lymphadenoma as well as Graves's disease, thymus enlargement is commonly if not invariably present. Here is a remarkable coincidence. Now Dr. John Orr has published a case of lymphadenoma which was cured by the administration of thyroid extract after other means had failed. In view of these facts it is impossible not to make the deduction that the lymphatic glands certainly, and probably the thymus also, may come to the rescue of the thyroid gland when the secretory capacity of the latter is overtaxed, or inefficient. But in lymphadenoma thus arising, the result is comparable with that in the old fable of the bear who was keeping the flies away from his sleeping master's face. One fly returned again and again, with the accustomed pertinacity of its kind, till the bear in desperation killed it with a blow of his paw, as it rested on the man's cheek. Thus the lymphatic glands in their well-meant endeavours to assist the thyroid may kill the patient with the disease which we call lymphadenoma. More scientifically expressed, I wish to infer that lymphadenoma is the result of a

futile attempt on the part of the lymphatic glands to resist the invasion of a poison (probably microbic in origin) which an efficient thyroid would never have allowed to pass its portals. Conversely it is possible that Graves's disease is merely the result of a well-meant endeavour on the part of the thyroid to do work which should have been carried out by the lymphatic glands. The enlargement of the thymus in each case looks as though that gland were capable of assisting either the thyroid or lymphatic glands when these structures are being worked to their full capacity, On the other haud, some have thought that the thymus is in some way antagonistic to the thyroid, and enlarges in Graves's disease in order to protect the body from the mad career of the thyroid gland. The same argument could be applied to the case of thymus enlargement in lymphadenoma. Thymus has been administered in Graves's disease with some success, as a supposed antidote to thyroid secretion. So far as my own brief experience goes, the action appeared to be beneficial in some slight degree, but I thought it was responsible for a rise in blood pressure. But granted that thymus is beneficial in Graves's disease, it does not follow that the two secretions are antagonistic. Thymus is certainly far less toxic to the organism than thyroid,

and the explanation of the benefit may very well be that the administration of thymus in Graves's disease does some of the work which the thyroid is so viciously engaged upon, and thereby actually lightens the labours and secretions of the latter, with a corresponding decrease of thyroid toxæmia. There is no doubt that all the internal secretions of the body are interdependent and complementary. All have their allies and opponents, and naturally each has some property peculiar to itself, as well as properties which can in time of need be supplied more or less (generally less) successfully by other glands. But the excessive activity of the deputy gland, though it may partially fulfil the foreign function which it is attempting to perform, may result also in an excessive production of its own peculiar secretion, and give rise to the disease which we recognize by such activity.

In the light of Dr. John Orr's case of lymphadenoma, it might be worth while to try the converse effect, namely, lymphatic gland feeding in Graves's disease. In this case it would presumably be some internal secretion of the lymphatic gland that would be required, and might possibly be preserved in a dried but active condition in the prepared gland. This gland feeding has been tried for tuberculosis, on the ground that sheep are very

immune to the tubercle bacillus, and hence it was argued that the bronchial glands, which would form the first or second line of defence in case of pulmonary infection by the tubercle bacillus, might possess some special antitoxic power. One observer is quoted by the purveyors of this gland preparation as saying, "The remedy must be used with caution in Graves's disease," as he had seen ill effects produced. Now this observation is at any rate evidence that the dry gland has active powers akin to those of the thyroid, and therefore in suitable doses it should be beneficial, if by any chance Graves's disease is merely the result of a well-meant but mistaken attempt of the thyroid gland to do the work of the lymphatic glands. It would also obviously be useful, if there be such a thing as lymphatic inadequacy. In a recent *post-mortem* that I was privileged to see on a case of Graves's disease that succumbed a few days after operation, there were no enlarged lymphatic glands, all that could be found being exceedingly small. But there was only a six months' history of illness. The pancreas weighed $1\frac{1}{2}$ oz. instead of $2\frac{1}{2}$ oz., the average weight in the female, which is an interesting comment on the fact already noticed, that thyroid secretion exercises an inhibitory influence on the pancreas. I have observed a long-standing

case of Graves's disease in which the tonsils were practically absent, there being a distinct hollow in the situation normally occupied by these bodies. This case was probably an example of the effect which thyroid secretion has upon the tonsils. If excess of thyroid has a similar inhibitory effect on the lymphatic glands, which is not unlikely, we are furnished with a probable reason for the evil influence of thyroid feeding in tuberculosis. The lymphatic glands are absolutely the first line of defence against tubercle, as evidenced by their invariable enlargement in this disease. Any inhibitory influence which interferes with the defensive power of the glands might well encourage tuberculosis, though the thyroid probably forms the second line of defence in this disease.

CHAPTER IX.

Thyroid and Eczema.

Eczema is one of the many diseases for which thyroid medication has been advocated. In view of this fact, the history of the following case may prove interesting. The patient was a child of 4 years and 10 months. He had been weaned when 3 months old, and eczema immediately appeared and has been troublesome ever since, sometimes better and sometimes worse. After weaning he was fed on condensed milk, milk and barley water, Mellin's Food, Allenburys' Food, and "all the baby foods" in turn; but at six months was so bad that he had to be put in a nursing home, where he stayed six weeks. He did not improve, however, so was taken into the country and fed on humanized milk, which seemed to suit him and he promptly got better. But the respite was not long, and attacks have been frequent ever since.

His eczema affected principally the genitals, perineum, popliteal spaces, wrists and face, with occasional outbreaks on thighs and abdo-

men. His scalp was not affected. Now the curious thing about this boy was the presence of many signs of abundant thyroid activity. His height was 3 ft. 6½ in., the average height of a child a year older. His weight 3 st., that is about 4½ lb. more than the average for his age. His pulse rate varied from 108 to 132, usually about 120, though he was not frightened or unduly excited, for we soon became friends. His teeth were perfect, without any sign of caries. He cut his permanent incisors (lower central) at the age of 4 years and 10 months, and the gums were already swollen with the unerupted lower "sixes." His bowels were open twice a day. He was sensitive to heat rather than cold, and preferred few bedclothes. He was very subject to small boils of the acne type. His hair was thick, though rather dry, and mentally as well as physically he was much ahead of his years. He had no enlargement of the tonsils nor symptoms of adenoids. He was constantly saying "I'm so tired," or "I'm so thirsty." I have already commented on thirst as a symptom frequently present in thyroid inadequacy, but it is also common in Graves's disease as is also the sensation of fatigue. The boy was made much worse by certain articles of diet, especially eggs and fish. These invariably brought out a rash, of urticarial type, so far as I could learn,

though I never saw it, and as a matter of course these articles had been long excluded from his diet. Now the whole group of symptoms in this case presented a remarkable contrast to the clinical aspect of thyroid deficiency, and I think one might fairly infer that thyroid activity was certainly in excess of the normal. I am sorry to say that the results of treatment were too conflicting to make satisfactory deductions. But an incidental attack of influenza, accompanied by vomiting and diarrhœa, with passage of mucus and blood, and of such severity as to necessitate the services of a trained nurse cured his ezcema temporarily. During the illness he was fed on Panopepton and sherry whey, his medicine for the most part consisting of mist. cretae. With Benger's food and a gradual return to his ordinary diet, the eczema again broke out, and a few weeks afterwards was worse than ever. So far as the eczema was concerned thyroid treatment was a failure, but the eczema appeared worse when thyroidism was either excessive or insufficient, and was less troublesome when a happy medium was maintained. His eczema only got well when his intestine was thoroughly empty, the child remaining in bed and living only on small quantities of the most digestible food. This was the only time when I succeeded in getting

a pulse count of less than 90, and I think one might fairly assume that there was a period of thyroid depression after this acute attack. That this was so we had further evidence shortly afterwards, for he wetted the bed on several occasions. But in spite of this the eczema had returned with convalescence, and though the administration of thyroid speedily stopped the enuresis and improved his general health, his eczema got steadily worse. The upshot of it all was that eczema was bad during a period of thyroid hyperactivity, and also during a time of thyroid depression.

The conclusion which I was bound to come to in this case was, that eczema was neither cause nor result of thyroid activity, though probably some toxin which was responsible for the eczema incidentally stimulated the thyroid gland, which in this case was able to respond, producing rather remarkable results in the growth of the child both physically and mentally. It is equally evident that a different result might have been produced, namely, thyroid exhaustion, and therefore it may often happen, that an individual who suffers from eczema may have become a thyroid deficient, and the administration of thyroid would in such a case be of immense advantage, possibly assisting the organism to such an extent that the eczema might get well,

though in this particular case neither the patient's own ample secretion nor an artificial supply proved effective. As to the effect of individual drugs, it is still harder to draw conclusions, because results obtained might have depended on other factors. But particular care was taken not to alter the local treatment, or the diet, when attempting to gauge the effect of any particular drug. Nevertheless, the following conclusions must not be taken as final, though the evidence was carefully weighed. Calcium lactate given three times a day for two days in 10-grain doses was beneficial to the eczema. If continued for more than two days it did harm, and equally, continuous small doses of calcium lactate did harm. Calcium iodide caused an immediate aggravation of the eczema. Arsenic was not given a prolonged trial, but on the whole appeared to have an unfavourable influence. Thymus at first gave good results, but was disappointing, The eczema certainly improved at first, and the bowels became constipated. The child remained thirsty. He complained that his nose had become stuffy and his tonsils began to enlarge. This, unless mere coincidence, obviously was combating the thyroid secretion, either by antagonism or inhibition, and was tried for a fortnight. At the end of that time he was

not so well in general health, and eczema began to get steadily worse again. So thymus was dropped. The dose used was equivalent to 2½ grains of fresh thymus three times a day. Then a change in the diet was prescribed, and he was put on a diet devoid of milk, cream, butter or animal fat, similar to that already mentioned in the case of Graves's disease. This was undoubtedly beneficial to the eczema. It did not appear to hurt the child, though obviously it is contrary to all our preconceived notions of what a child's food ought to be. He was allowed fruit, vegetables, lean meat and soups. His weight altered very little, showing first a gain of 4 ounces, and ultimately a loss of 9 ounces during eighteen days of this diet. During this time he was very well in general health, appetite good, bowels inclined to be constipated. His pulse on one occasion dropped to 99. At the end of the eighteenth day, however, he fell a victim to influenza, as already mentioned, and with further evidence that the thyroid was not responsible for his eczema, either by faults of omission or commission, there was no justification for returning to this abnormal diet. The moral of the whole case is that thyroid activity is Nature's method of dealing with certain toxins (which in this case were the cause of eczema), and therefore in

some cases where the toxins have gained the upper hand, the thyroid secretion is possibly inadequate and may be usefully supplemented. This is of course the *rationale* of the thyroid treatment of rheumatoid arthritis, which is probably due to toxins of intestinal origin. Other debilitating influences have frequently been noted. These may very well induce thyroid exhaustion and so allow full play to toxins, which might be efficiently dealt with by an adequate thyroid. It is interesting to note that Garrod relies largely on iodide of iron in this complaint, iron and iodide both being drugs which stimulate or assist thyroid activity, whilst other authorities rely on the intestinal disinfectant guaiacol carbonate. In view of these facts, it seems highly probable that there may often occur paroxysmal periods of thyroid activity, or exhaustion brought about by the vicissitudes of life. I am disposed to think that acne spots of youth are probably due to hyper-activity of the thyroid gland. All honour to the staphylococcus and acne bacillus, but a few doses of iodide or bromide of potassium will often produce a similar result. These spots are essentially a feature of youth, and have a tendency to disappear as the adolescent develops into the adult, that is to say, they are most prone to occur during the periods when there is a big reflex discharge of thyroid activity.

Dr. Arnold Lorand tells us (in an article published in the *Lancet*, November 9, 1907) that he was particularly subject to acne during ten months when he was experimentally taking thyroid. The little boy whose case I have just described was also very subject to isolated large acne spots, or small boils, according to the nomenclature one may prefer. May they not be caused by excess of iodine poured into the system by the thyroid? It is a significant fact that arsenic is the best remedy for acne (except, of course, vaccine); arsenic here acting as an antidote for thyroid secretion. One difficulty in this view is that Graves's disease does not usually present the worst cases of acne, though a minor tendency to acne is often present. But it may be merely a question of dosage. One remedy for the symptoms of iodism, if they occur during the administration of potassium iodide, is to double the dose. In Graves's disease the dose of thyro-iodine is probably much more than doubled. Also it may be that the staphylococci of suppurative acne do not thrive any better than other disease germs do, under the influence of the prolonged thyroid activity of Graves's disease. The victims of Graves's disease are usually remarkably immune from ordinary infections. It is highly probable, however, that in the adolescent cases of which we are speaking,

thyroid activity is paroxysmal and irregular rather than continuous, being modified, among other circumstances, by the irregularities of sexual development. Possibly paroxysmal thyroid activity, and resulting temporary exhaustion, may be responsible for some of the curious anomalies with which we are sometimes confronted. A patient whose total thyroid secretion is apparently plus, will from time to time exhibit some symptom which we are accustomed to associate with the minus condition. Even Graves's disease presents some anomalies of this kind, and the fact that some cases end in myxœdema or complete thyroid exhaustion lends support to the above explanation. Thirst, ravenous appetite, loss of hair, dental caries, various pigmentary changes in the skin, urticaria, a constant sensation of fatigue and inability for exertion, hæmorrhages, disorders of menstruation are all symptoms that may be met with in Graves's disease (Allbutt's "System of Medicine"), and I have seen all these symptoms definitely improve in various thyroid deficients under the influence of thyroid medication. In the case of dental caries, of course, it is needless to say that carious teeth did not improve, but in these children, though the deciduous teeth had been very bad, the permanent teeth showed every sign of being good. A tempting explana-

tion of these anomalies, when met with in Graves's disease, is to suppose that in spite of continued thyroid hyper-activity the secretion may have deteriorated in some of its properties, and thus given rise to some of the symptoms which we are accustomed to associate with thyroid inadequacy. I have seen chilblains occur in a patient recovering from Graves's disease, and speedily relieved them with a prescription containing calcium lactate, liquor arsen. ♏iv. and gr. i. of thyroid, taken three times a day. But the symptoms of Graves's disease were increasingly aggravated each day that the patient took this mixture, and in three days it had to be left off.

CHAPTER X.

Thyroid and Arsenic.

Arsenic is a drug which undoubtedly has a special influence on thyroid activity. Precisely what that influence may be is a matter that demands careful consideration. Many observations have been made on the subject, and the results appear somewhat conflicting. I have seen it stated that arsenic is a normal ingredient of the thyroid gland, and that it is sixteen times as plentiful in the human thyroid as in that of the sheep. But there are obvious difficulties in accepting a statement of this sort, in the face of the fact that expert analysts, accustomed to dealing with thyroid substance for the market, failed to find any trace of arsenic when testing a large quantity of sheep's thyroid. Arsenic, as is well known, has a great tendency to remain in the body a long time after it has been taken by the mouth, and may readily be detected in a corpse long after burial. Now, most human beings take arsenic at some time during their lives, and town dwellers probably inhale a

small quantity daily in our smoky atmosphere; not to mention the amount we used to take in our beer, and probably also in many other ways of which we know nothing. Therefore, when analysis detects infinitesimal quantities of arsenic in the thyroid or any other organ (and it has been found in most organs), it is somewhat difficult to say whether it is proper to the gland or merely retained there. One might equally well say that carbon is a normal ingredient of the human lungs. In a sense this is true, inasmuch as it is invariably present. Further, seeing that arsenic has a special influence on thyroid activity, it is not unlikely that the gland may possess a selective action for arsenic, and so retain more of it than is the case with other organs. The very difference in the amount of arsenic found in the analyses of the human and the sheep's thyroid makes it all the more probable that the matter depends largely on food and chance circumstances. The sheep, living in the country for the most part, are less likely to obtain arsenic from the smoky atmosphere. And, on the other hand, the food of man, which is so largely manufactured and artificial, has infinitely more chance of getting contaminated with arsenic than that of the sheep. But even sheep are to some extent artificially fed, and arsenic may sometimes find its way

to their thyroid glands in some purely accidental manner, which might readily occur if arsenic were an ingredient of a sheep dip or any preparation used for other purposes in tending the flock. But perhaps it is not a matter of great practical importance whether arsenic is a *normal* ingredient of the thyroid gland or not, though a knowledge of this matter might help to decide some other problems. I believe it is generally held that it is a normal ingredient, in extremely minute quantities. In any case, it seems highly probable that arsenic owes much of its therapeutic effect to its action on the thyroid. Minute doses increase the rapidity of the pulse. That may well be by neutralizing a small quantity of thyroid secretion and thereby stimulating an increased production. Large doses diminish pulse frequency, which may well be by neutralizing a larger quantity of thyroid secretion and for the time being depriving the body of it. It would be interesting to have some reports on the condition of thyroid secretion in the arsenic eaters of Styria. Their ability to undergo prolonged exertion without fatigue might possibly be due to special excellence of their thyroid glands, whose powers of secretion might be augmented by this daily course of arsenic. It is well known that muscular fatigue is very rapidly induced in thyroid inadequates,

and also that muscular exercise depresses thyroid activity. The deduction is, that it is the duty of the thyroid gland, among other things, to eliminate fatigue products. Therefore, the better the thyroid the less fatigue. Why then cannot the victims of Graves's disease undergo fatigue? The answer appears to be that in their case the thyroid is already working at full pressure, and any cause which called for further activity would naturally make the patient worse. As a matter of fact, even in Graves's disease there is ample evidence that muscular exercise does increase thyroid activity, aggravating the symptoms to such an extent that the patient is bound to desist. But arsenic has long been a standard drug in the treatment of Graves's disease. Is this by neutralizing thyroid secretion? or does it improve the general thyroid tone by giving gentle exercise, in the same way that graduated exercise may improve irregular and failing hearts? Arsenic is also the standard drug for lymphadenoma, psoriasis, chronic eczema and acne, all of which conditions at times appear to be related to thyroid activity. Thyroid medication has proved successful in cases of the first three disorders, so the utility of arsenic in these complaints might be explained on the ground that it stimulates thyroid secretion, or perhaps one ought to say, improves thyroid capacity.

The power of arsenic in preventing acne, whether induced by bromides, iodides, or of obscure origin, is difficult to explain, specially in view of the fact that thyroid feeding may be productive of acne. The last factor and the utility of arsenic in Graves's disease suggest that the drug is antagonistic to, or neutralizes, thyroid secretion. Further, some observers find that the unpleasant symptoms of thyroidism may be prevented by prescribing arsenic and thyroid gland substance together. Unless this is to be described as irrational pharmacy, the administration of substances having opposite effects, we must find some rational explanation.

The only explanation I can think of which fits the case, is that the arsenic when administered takes charge of the iodine (possibly by chemical combination), and so acts as a sort of guardian or trustee for the affairs of the thyroid, serving out thyro-iodine with a careful hand. Thus, under the influence of arsenic the iodine is not allowed to be wasted and excreted by the skin in acne pustules. There is less iodine allowed to flood the system in Graves's disease, naturally resulting in improvement. By careful management there is a supply of reserve iodine kept in the thyroid store for emergencies, such as the prolonged muscular exertion of the Styrian

arsenic eaters. Similarly, thyroid efficiency may be increased, and the organism enabled to deal with eczema, psoriasis, or lymphadenoma. And when additional thyro-iodine is fed into the body, the arsenic immediately assumes control and doles it out with careful hand, so preventing symptoms of "thyroidism." This hypothesis would also account for a fact which I have noticed several times, namely, that goitres decrease more rapidly under the influence of thyroid feeding alone, than when arsenic and thyroid substance are administered together. The immediate effect of administering arsenic with thyroid is equivalent to lessening the dose of thyroid, because the arsenic, so to speak, ties up some of the available iodine, however badly this may be wanted in the system. At the same time, it seems to stimulate the thyroid gland to greater exertions, and in consequence one sometimes sees an actual enlargement of the goitre under its influence. There are obvious objections to stimulating an enlarged thyroid, and for this reason one would prefer not to give either arsenic or iodine to patients with goitre, as a general rule. Personally, I would endeavour to do all the work of the enlarged gland and let it lie dormant and atrophy. When it has shrunken to due proportions one can stimulate, if necessary, without fear of launching

the patient into potential Graves's disease. One must however bear in mind the possibility that there may be an actual shortage of iodine in the system, and therefore an occasional dose, say a one-grain iodoform pill, might be administered with advantage. This dose may appear ridiculously small, but in reality is not so. It has been shown that iodoform has an even more powerful influence than potassium iodide on thyroid activity. Iodoform contains more iodine than potassium iodide, a single grain of which represents approximately the amount of iodine contained in thirty-eight grains of thyroid tabloid. I had one patient, the subject of goitre, who showed marked improvement after the omission of the one grain of potassium iodide, and one minim of liquor arsenicalis which had been administered with 1½ grains of thyroid three times a day. The thyroid was continued alone and followed by a much more rapid increase of weight and sense of well-being, and a more rapid decrease of the parenchymatous goitre. This particular patient had a large goitre with a tendency to hyper-secretion. If it be decided to give iodine in goitre, small doses are better than large. Chemically, a small dose is fully adequate, and the thyroid has the chance of helping itself to all its wants, and clinically it has been shown that small

doses are actually more potent than large. When large doses are administered, probably the iodide acts more as an irritant, and more rapidly sets in motion the apparatus for its own elimination, which is chiefly done by the kidneys. There is also the possibility that it fatigues and exhausts the thyroid by over stimulation, so that actually a less quantity may be absorbed. Probably, this is why small doses of iodides are more prone to cause iodism than is the case with large doses. The small doses being administered to the body viâ the thyroid gland cause many of the well-known symptoms associated with hyper-thyroidism, headache, quick pulse and looseness of the bowels. But when larger doses are given the kidneys get to work and eliminate it rapidly, so that the thyroid and other organs are not so troubled, and symptoms of iodism are absent. It would appear probable that those who are hypersensitive to the administration of iodine are the possessors of unusually active thyroid glands, and this inference may prove of value in giving one a fuller understanding of the patient. Persons suffering from Graves's disease have been observed to become worse under the influence of sea air, and this fact has been explained by the assumption that the iodine present in sea air was sufficient to aggravate

the symptoms. Considering the very minute quantity of iodine present in what may be considered a normal daily secretion of thyro-iodine, this theory is by no means so ridiculous as it seems. But, on the other hand, it has been noticed that neurasthenics as a class do not do well by the seaside, so it may be the neurasthenic element of Graves's disease which is unfavourably influenced, rather than the iodine factor. Trousseau found, however, that iodides produced acute paroxysms of the disease. In this connection it is worth considering all complaints which are powerfully affected by any form of iodine or of arsenic, to see whether such action may be influenced by thyroid secretion. Now mention has already been made of the value of arsenic in lymphadenoma, and it has been authoritatively stated that arsenic is the only drug which has any influence on this disease. But in the more modern light of Dr. John Orr's success with thyroid, I have just suggested that this beneficial action of arsenic in lymphadenoma may be at least partly due to the special action of the drug on the thyroid gland, though one must not, of course, lose sight of the effect of arsenic on particular micro-organisms.

Most observers seem to be agreed that arsenic stimulates thyroid activity, though the conclusion to be drawn from the various

uses of arsenic which I have enumerated would rather be that on the whole arsenic controls thyroid activity, though it may increase thyroid capacity. Perhaps it is not fair to draw conclusions from the action of arsenic in diseases like eczema and psoriasis, owing to the special influence of arsenic on the skin; though even that might be by way of the thyroid gland. It is probable also that arsenic has its own controlling influence on lymphatic secretion generally, being the only drug of value in lymphatic leukæmia, as well as in lymphadenoma. And this influence might also play a part in the effect of arsenic on Graves's disease, in which malady, as already mentioned, the lymphatic glands may have a share. But there is another most interesting use of arsenic in medicine, namely, in treating consumption. Various authorities are agreed that Fowler's solution is probably the most generally useful remedy in this disease. And, on the other hand, Leonard Williams says that for some reason thyroid is very badly borne by consumptives, and hence must be given with great caution, or not at all, where there is any suspicion of this complaint. It appears in some cases to do very definite harm, though in others it has been given with impunity, and benefit to the condition for which it was administered. Recently, cases

of inoperable cancer have been considerably benefited by thyroidectomy. Stuart Low, the author of some such successful operations, finds evidence of excessive thyroid activity both in carcinoma and tuberculosis, and speaks of the thyroid as the fly-wheel of body growth and metabolism. If the fly-wheel revolves too fast, excessive metabolism leading to wasting will naturally result. This is the argument against the administration of thyroid in tuberculosis, and incidentally in cancer. It may be that the beneficial influence of arsenic in tuberculosis is due to its restraining action on the thyroid. The same factor would account for the fattening action of arsenic, and, perhaps, also for the good effect of calcium in tubercle. It must be noted that although the immediate effect of arsenic probably is to stimulate thyroid activity, it has to be administered for extended periods to produce its therapeutic effect in the diseases for which it is used as a remedy, such as Graves's disease, lymphadenoma, tubercle, pernicious anæmia, psoriasis, chronic eczema, and so forth ; and it is also only by prolonged administration that the Styrian peasants are able to gain their immunity from fatigue. Except for the case of the latter, one would be tempted to say that the action of arsenic on the thyroid is to all intents and purposes

suppression, and that though the thyroid may at first attempt to resist (manifesting symptoms of activity), very soon the arsenic gains the upper hand, and exercises mainly a controlling influence. If we add that arsenic increases thyroid capacity, I think this explanation will fit all cases, though I do not necessarily wish to infer that arsenic has no action apart from thyroid influence. Arsenic has been administered for epithelioma, rodent ulcer, and even scirrhus (Ringer and Sainsbury). Surely this was a step in the dark towards Stuart Low's thyroidectomy. The curious thing is that in tubercle and cancer Nature's attempts to fight the toxins (which she does by instituting special thyroid activity, as we can demonstrate in the *post-mortem* room) should be not only futile, but positively injurious. Probably the proper way to regard the matter is that up to a certain point, namely, in the early stages, thyroid activity is beneficial, and may even help to attain a successful issue in those cases in which the battle is won. But the thyroid does not know when it is beaten. It is no use to bring up the whole of our resources against overwhelming odds. It only makes defeat more signal, and makes any ultimate rally impossible. Arsenic is also "often serviceable in rheumatoid arthritis," says Ringer and Sainsbury's "Handbook of

Therapeutics." "All forms may be cured, but it sometimes fails, and indications for its employment are unknown." One might suggest that it succeeds in those cases in which the thyroid is able to make an adequate response to arsenical stimulation. The same authorities state that arsenic makes the bones heavier and more compact. It is probable that it assists the thyroid in the duty of calcification. Phosphorus has the same effect so far as the bones are concerned, and possibly for the same reason. The general action of phosphorus in medicinal doses, and its value in rickets, both suggest that it also has considerable influence on thyroid activity. There is another disease for which arsenic is a standard remedy, namely, asthma. And in treating this complaint, iodides have a place of perhaps equal importance with arsenic.

In view of these facts it is worth while to see what influence thyroid has on asthma. I feel sure that I have read somewhere that asthma is one of the many possible results of thyroid deficiency, but cannot now trace the source of this statement. I have treated several patients on this supposition with varying success. Asthma of course depends not infrequently on nasal conditions, which again are frequently the result of or associated with adenoids. Here is obviously an argument

that thyroid treatment will do good. There is also a widely prevalent (but probably erroneous) notion, that asthma is due to a sort of urticarial condition of the bronchial mucosa, which in itself, or by provoking spasm of the bronchial muscles, causes the paroxysm. The supposed urticarial condition might very well yield to calcium salts and thyroid, one or both. But, as pointed out in a recent article in the *Practitioner*, asthma cannot be due to obstruction of the bronchial tubules by any urticarial swelling, inasmuch as during the paroxysm of asthma the sufferer is able to inspire air freely, but the difficulty is an expiratory one. Hence, the chest gets into a highly distended emphysematous condition and the air wheezes out slowly, If the difficulty were due to mechanical obstruction by turgid mucous membrane, there would obviously be equal difficulty during inspiration and expiration. The difficulty therefore depends on some more complex nervous mechanism, which apparently induces spasm as soon as an expiratory effort is made, but leaves the inspiration free. Such a condition may be compared with sobbing, which is the physiological opposite. A sob consists of a series of short spasmodic inspiratory efforts, which may be followed by a prolonged free expiration or sigh. Again a laugh is a series of spasmodic expiratory

efforts, accompanied by phonation or not, according as the vocal cords are brought into play or otherwise. Curiously, hilarious laughter may provoke a spasm of asthma, as I have witnessed in a susceptible subject. But though the paroxysm of asthma cannot be due to mechanical obstruction caused by an urticarial condition of the mucosa, it is still possible that such an urticarial condition may exist and be the starting point of the nervous paroxysms. Whether this be so or not, it is by no means uncommon to meet with other signs of thyroid deficiency in the victims of asthma, and accordingly appropriate treatment will certainly be beneficial to the patient, and in some cases health may be so improved that the asthma quickly gets well. I have had several such cases, but at the same time it must not be expected that thyroid treatment will prove a panacea for asthma. On the other hand, prolonged asthma, like most other depressing conditions, undoubtedly has an unfavourable effect on thyroid metabolism, and in such cases attention to this point has given me striking results, though as a remedy for asthma pure and simple I confess that thyroid has disappointed me.

CHAPTER XI.

The Influence of Salicylates and Kindred Drugs on Thyroid Activity.

This subject involves of necessity some consideration of thyroid activity in relation to fever. It is a tempting theory that the ordinary symptoms of fever are due, at least in part, to increased thyroid activity, such activity being one of Nature's methods of dealing with toxins which may have obtained access to or been formed within the body. Evidence in favour of this supposition has been supplied by Roger and Garnier, who found that in acute infectious diseases with fever there is increased thyroid activity with enlargement of the folliculi, which are filled with a large quantity of colloid substance. Further, we have ample evidence that thyroid exhaustion is commonly manifested by clinical symptoms as a sequela of febrile diseases. Dr. Arnold Lorand has discussed the whole matter in a most interesting article, which appeared in the *Lancet* of November 9, 1907, and throughout that article he certainly cannot be accused of under-rating thyroid influence.

He attributes the rapid pulse, abundant perspiration, polyuria and diarrhœa all directly to thyroid influence, and quotes experiments to show that the rise of temperature may very well be due to the same cause. The supposition is attended with certain difficulties, and if we accept it we shall be driven to certain other logical conclusions. Throughout we shall take Graves's disease as our standard of excessive thyroid activity. Now the process of fever is not a solitary and simple condition, but a complex cycle of events which tends, however, to follow a fairly definite course. Accepting thyroid activity as the main factor, we shall attempt to interpret events as we go along. Firstly, there is a sensation of lassitude and chilliness, which is probably a signal that toxins have gained access to the system, which has used up all the available thyroid secretion in attempting to neutralize them. And though the thyroid sets to work with all diligence to make more, for a time the secretion is neutralized by the toxins as fast as it can be produced. Thus, there is a period of temporary thyroid deficiency in spite of rapid production. The deficiency accounts for the sensation of cold, often amounting to actual shivering, and also for the constipation which is so frequently present. It may also account for the want of appetite, so often observable

in patients who suffer from thyroid inadequacy, and possibly even for excessive thirst, which I have likewise often noticed in similar cases, and have already noted elsewhere. A corresponding point about the thirst is that cold water is the drink preferred to any other, a fact which may be readily verified by inquiries among half a dozen children suffering from minor degrees of thyroid inadequacy. On the other hand, we must assume that thyroid activity is in itself the cause of the increased pulse rate and rise of temperature. The flushed face, the sensation of throbbing carotids and temples, and the consciousness of every heart-beat, are all familiar features both in Graves's disease and fever. The tremor and sensation of fatigue will be equally witnessed in both conditions. But as yet we have no sweating, which is almost invariable in Graves's disease. In fever this occurs later and with it the fall of temperature. On the other hand, pyrexia is by no means a constant feature of Graves's disease. Here are two difficulties which require careful handling, and have possibly proved a stumbling-block to some who might otherwise have accepted this theory before. The difficulty can be got over by the following explanation. A rise of temperature, not necessarily amounting to pyrexia, is the immediate effect of big doses of thyroid,

whether administered by the mouth or by sudden hyperactivity of the patient's own gland. Pyrexia is prone to occur, when the surgeon unintentionally floods the system with thyroid secretion, by manipulation of the gland during operation. But sweating only occurs when the organism finds itself flushed with more thyroid secretion than is required. Thus in Graves's disease, where secretion is in excess all the time, sweating is the rule. Again during active exercise there is evidence of increased thyroid activity, shown by increased pulse rate and flushed skin, but sweating does not immediately occur, perhaps not till secretion is in excess of demands, the first supplies being presumably taken up by fatigue products. And in fevers, when the production of thyroid secretion exceeds the amount required to neutralize the toxins, sweating occurs, followed by a fall of temperature. The improved condition of the patient is fully in accordance with this view. The fall of temperature is partly regulated by evaporation of sweat, but probably depends still more on reflex inhibition or temporary exhaustion of the thyroid gland, which has now succeeded in the task it set out to perform, namely, neutralizing the toxins, producing secretion enough and to spare. The temperature often falls without the occurrence of sweating, and will frequently remain low,

with a correspondingly diminished pulse rate, for several days. The duration and severity of the symptoms will naturally depend on the amount of toxins produced, and the capacity of the thyroid to neutralize them in a longer or shorter time. The dose may of course be more than the thyroid can deal with, or hyperpyrexia may result from excessive thyroid activity. Such contingencies do not affect the argument as a whole, and it may be fairly claimed that the position is at least not untenable.

Similarly it has been argued that salicylates (and presumably other antipyretics) produce their effects by thyroid stimulation. A moderate dose of salicylate of soda in the healthy subject produces (according to Mitchell Bruce) "increased cardiac action, flushing and warmth of the surface with perspiration," and other symptoms which are to some extent peculiar to the drug. So far, this may very well be explained on Dr. Arnold Lorand's assumption that salicylate of soda acts by stimulating thyroid activity. And in fevers, when thyroid activity is already high, a dose of salicylate of soda may still further stimulate the gland, and so hasten the sweating and general abatement of the symptoms. Whether the proceeding is beneficial or not is quite another matter, and involves the whole ques-

tion of uses and abuses of antipyretics. The patient feels better with a fall of temperature and a good sweat, but sometimes the temperature rises again, bringing back all the previous discomfort; and in this case we may well wonder whether we have been premature in our efforts or not. In theory, of course, when the illness is commencing, and toxæmia still slight, if by a few doses of salicylates or other antipyretics we can hurl into the circulation enough thyroid secretion to form antitoxins or annihilate the germs by whatever mode is usual, we may then congratulate ourselves on having cut short the attack. How be it, our method may have been extravagant, and if we have miscalculated the hidden forces arrayed against us, we may have committed a grave strategical error which, perhaps, would not have been done by Nature unaided. It is, of course, possible, or even probable, that salicylates have an action which is hostile to micro-organisms, or even poisons of other origin, and that benefit accrues from such action quite apart from thyroid influence. But the point I wish to lay stress on is that salicylates have a powerful influence *against* thyroid activity. In view of what has just been said, this seems a startling statement, and therefore requires proof. Whether salicylates powerfully stimulate, and so rapidly exhaust thyroid

activity, or whether they actually neutralize it, which in the case of an active gland would stimulate further production (like lemon-juice and saliva, or alkalies and gastric secretion), I cannot say, but the evidence I am about to bring forward points to the latter conclusion. I will quote three cases. J. D., a robust adult, had an acute tonsilitis. He had stuck to his work for three or four days when I first saw him one morning. He had then taken to his bed with a pulse rate of 120, and temperature 102° F. He had headache, and aches and pains in the limbs severe enough to suggest rheumatism, but possibly only influenzal. He was given a mixture containing 15-grain doses of sodium salicylate and half-drachm doses of compound tincture of cinchona. But owing to variations in the size of the domestic tablespoon, he took repeatedly a larger dose, roughly 20 grains of salicylate and 40 minims of bark every four hours. The error was not discovered for thirty-six hours. He then had a (morning) pulse rate of 48, and temperature of 96·4° F. He had sweated profusely the first night, and his bowels were obstinately constipated, resisting strong doses of aperient. The pulse and temperature remained at this low level all the next day, and the bowels were still obstinately constipated in spite of aperients, though the salicylate mix-

ture had been left off. Thyroid, $2\frac{1}{2}$ grains twice a day, was then given for two days, and the temperature again rose, this time to nearly 101°, and pulse to 98. The throat progressed rather slowly, in spite of energetic antiseptic treatment, which had given me excellent results in other cases. The patient returned to work twelve days after I first saw him, when, in spite of full doses of strychnine, he had a very soft dicrotic pulse of 76 and a blood pressure of only 100 mm. Hg. I have already mentioned that this patient was usually robust, and may add that ordinarily his bowels were remarkably regular. The low pulse rate, the dropped temperature and obstinate constipation, all suggest that in this case the thyroid was seriously depressed by the drugs mentioned. The low blood-pressure was probably due to the same cause, inasmuch as high blood-pressure is a common feature of Graves's disease. If this interpretation be correct, it is probable that the heavy doses administered did harm and prolonged convalescence.

Case No. 2 was a woman of 39, who had suffered from life-long constipation, and manifested the ordinary signs of thyroid inadequacy. Her general condition had been enormously improved, and constipation much lessened by thyroid medication. On one occasion her bowels had been perfectly regular for over a

week without any medicine other than thyroid, and she could not remember that this had ever occurred before. At the time of which I now write she was taking a small dose of cascara nightly, and was somewhat tired, owing to disturbed nights entailed by her duties as nurse. She was given aceto-salicylic acid for a slight attack of lumbago, and though the dose did not at any time exceed 10 gr. thrice daily, her constipation greatly increased, and the nightly dose of aperient medicine had to be more than doubled while taking this drug. It is only reasonable to suppose that the increased constipation was due to exaggeration of the thyroid depression caused by the aceto-salicylic acid.

Case No. 3 was one of Graves's disease. I had previously found aspirin to be of great value in controlling paroxysms of tachycardia, and accordingly prescribed a daily morning dose of 10 gr. for this patient, who usually had an attack of palpitation after breakfast. The remedy was perfectly successful, and in view of the cases just quoted I resolved to try the effect of three or four doses daily. The result was rather remarkable, and more than justified my expectations. The pulse-rate improved considerably, and the patient felt very much better. Her bowels, which had previously been open twice, and often three times a day, were now open but once daily. She increased

2 lb. and 1 oz. in three days. Though this increase in weight might be attributed to fæcal accumulation, it does not affect the argument, inasmuch as the previous intestinal activity was due to excessive thyroid action. The only objectionable feature was some gastric disturbance, which may have been caused by using a less pure substitute for aspirin. Sweating was, if anything, less than previously. More prolonged experience of this treatment is necessary before one can pronounce final judgment, but I think it proves that aspirin, and possibly other salicylates and allied drugs, will be found of inestimable value in Graves's disease. One might avoid the gastric disturbance, and possibly get still better results, by local use of one of the easily absorbed salicylic compounds directly applied to the skin over the thyroid gland. The final result naturally depends on whether thyroid control or exhaustion will cure Graves's disease or otherwise, which is quite another question, and has already been discussed.

Further, in view of the beneficial results recently obtained by thyroidectomy in inoperable cancer, similar benefit might be obtained by the use of aspirin in such cases, many of which are also unsuitable for thyroidectomy. Aspirin has of course been used for the relief of pain in cancer, and this may explain the *modus operandi.*

CHAPTER XII.

General Considerations.

THERE is another class of patients who are frequently much benefited by thyroid treatment, though in their case a cure cannot possibly be expected, which is in itself a sufficient reason for doing all we can to alleviate them. I refer to the large class of degenerates, whose cases of course vary enormously in detail. I do not wish it to be understood that I look on thyroid deficiency as a cause of their degeneracy, but an examination will surprisingly often show that it is a very important concomitant factor. This result may, of course, be brought about in two different ways: Firstly, the cause of degeneracy may also cause thyroid depression directly; and secondly, thyroid depression may very readily result from the inaction and unhealthy life which infirmity forces on the sufferers. I will quote two cases as examples. The first is a congenital idiot whom I commenced treating six months ago. Her age was then 6½ years, and from the history I have little doubt that her mother suffered from a

severe attack of syphilis several years before this child was born. The first child was healthy, then followed four or five miscarriages, and then this imbecile. The child, when first seen, was able to say a few simple words, but rolled the eyes and head about in a horrible manner, and had loud snoring respiration. She exhibited unceasing movements, not only of the head and neck, but also of the arms and hands, especially the left. The movements differed from those of chorea, being far less jerky and spasmodic. She was not able to use the left hand for any serviceable purpose, owing to the constant movements, and though there was no paralysis, the hand was constantly hyper-extended and grossly distorted in many and various malpositions. I was told that the child suffered from paralysis, but the malady appeared to me to depend rather on want of co-ordination. The individual movements were strong, and there was no lack of power to grasp, or to flex or extend the wrist. The same lack of co-ordination possibly accounted for inability to stand. There was no deformity of the limbs, which were uniformly ill-nourished, but could be easily moved into any position desired. Intelligence appeared to be sadly deficient, and the child could not be left untended for a moment, except in bed. As to signs of thyroid inadequacy: she had an

operation for adenoids when ten months old. She had a high palatine arch, and nearly all the temporary teeth were badly decayed, many of them necessitating extraction. This was done under gas without difficulty. Her mouth was at first always open, and usually dribbling, but she could breathe without distress when it was held shut. She had a poor appetite, was very sensitive to cold, and suffered from chilblains. She had no excessive thirst, nor enuresis. Her hair was good, and had never been scanty. The bowels, at one time very constipated, were now more regular, and the new teeth (4 centrals and one "6") were good. Thus there obviously had been many signs of thyroid inadequacy, though the general tendency showed improvement. Nevertheless I resolved to give thyroid treatment a trial, and the result was far more satisfactory than one could have anticipated. The first thing noticeable was a great improvement in facial expression. She very soon obtained co-ordination of her oculo-motor muscles, and was able to hold up her head and look at anything straight, instead of rolling her eyeballs up into one corner or under the lids, with the head dropped on one side. She also gained much more control over her hands. As the mother expressed it, "she did not knock about near so much." She became much quieter and ate

better. In a month she was able to sit up in a chair, which she had never done before. She commenced to talk more, imitating her sister. She was soon able to sit up at table to have her meals, and according to the mother's statement, perceived if anything usually present were lacking from the table. In the history of a case like this, one is bound to accept the statements of the relatives as to improvement, because the child being at home, improvement is noticeable in a number of little things which do not occur under the eye of the practitioner. Thus, though I am able to see a vast improvement in the general intelligence of the child so far as appearance goes, and also a great lessening of the involuntary movements, the parent's affirmations as to general improvement are much more enthusiastic. And though we cannot look forward to the child's becoming a genius, the mother's statement that "she has never been so nice as she is now" is worth something, and in view of the past improvement I look forward with confidence to still further increase of intelligence with age and experience.

The second case I will mention is that of a girl, now 19, who had "a stroke" at the age of 11, affecting her speech centre and paralysing the right arm and leg. Before her calamity she was said to be a bright and

intelligent child, well advanced in her school. For some months she was silent and gave no sign of comprehension of anything that was said. Eventually she again learned to talk, and to write with the left hand. When I first saw her the parents said she was not so well as six months previously. She did not talk nearly so well, had given up her writing, and was more apathetic. Her speech was not exactly a drawl, but the words were uttered slowly and deliberately with long interspacing. Her teeth were bad. She was always constipated and perhaps a little unduly sensitive to cold, both of which symptoms would be natural to a paralytic. Now though the symptoms did not point strongly to thyroid inadequacy, there was no doubt at all that the administration of thyroid did her a lot of good. She was given 2½ gr. daily in divided doses, and not only her parents noticed a great improvement, but also her friends. The girl was much brighter and talked a great deal better. She told me herself she had been very bright all the week, and there was no reason to attribute the improvement to any other factor, because her routine life was unaltered, and I had only seen her once and did not hold out any delusive hopes of cure; so one could hardly attribute the improvement to suggestion, and it was

highly improbable that such improvement could result from the cheering influence of a solitary visit from a stranger.

Enough has now been said about thyroid secretion to show that there are a vast number of conditions in which good may rationally be expected from judicious thyroid therapy. Perhaps the most satisfactory cases will be those of minor thyroid inadequacy, especially in children. These cases are not difficult to diagnose with a little practice, and are exceedingly common. One of the most striking things about them is that often there is no tangible complaint to which a name has been given, and other lines of treatment have usually been tried and proved unsatisfactory. The symptoms as described by Leonard Williams have already been discussed and illustrated by an extreme case in Chapter I. In older people too, especially women, it is probably no exaggeration to say that thyroid inadequacy is just as common as anæmia, and equally important in its results. There is, however, this important difference, that nearly everyone can diagnose anæmia, whereas it takes considerable technical knowledge to diagnose thyroid inadequacy. So far as treatment goes, thyroid inadequacy is on the whole the more satisfactory condition, but often goes hand-in-hand with anæmia. As to dosage,

Leonard Williams' principle of giving the smallest dose found to be satisfactory, is certainly the best. For children, doses of ½ to 1 gr. t.d.s. will commonly be found effective. With adults, I have found a dose of 1 gr. three times a day usually satisfactory, but headache occasionally results even from this quantity, especially if combined with small doses of iodide.

The special actions of calcium, arsenic and iodides have already been discussed, and these drugs may be prescribed or withheld according to the judgment of the prescriber. I cannot say I am in favour of adding them as a matter of routine, though apparently such is the practice advocated by Leonard Williams, whose experience is of longer duration than mine. The duty of the thyroid in dealing with poisons such as may be formed within the body by disease is an argument in favour of administering thyroid at the onset of acute illnesses. But there is possibly a doubt whether thyroid administered by the mouth has the same power of neutralizing toxins as the naturally generated secretion. There is also the question whether administration of thyroid by the mouth may not exercise an inhibitory effect on the patient's own secretion. If such be the case, and thyroid tabloid be less efficient than the patient's own secretion, we may obviously be doing harm.

This might be a reason why tuberculous patients are sometimes made worse by thyroid. On the other hand, such an inhibitory influence might well be productive of good in cases of thyroid exhaustion by giving physiological rest to an overworked gland. The addition of arsenic, iodides or calcium would all theoretically tend to prevent inhibition of the gland's own activity, and that this is so I have proved for myself and accept as a definite fact. The theory of inhibition might even explain the failure to cure nocturnal enuresis when too large a dose of thyroid is administered, which Leonard Williams cautions us against. In this case, naturally, the larger the dose of thyroid, the more the patient's own gland would be inhibited. There may be some virtue in the patient's own thyroid secretion, not present in an active form in the dried preparation, which virtue saves the normal individual from the troubles of enuresis. A minute dose of thyroid substance administered by the mouth may possibly, by doing some other part of the thyroid's work, eke out the patient's own secretion for this purpose without exercising any inhibitory effect. But it is difficult to suppose that nocturnal enuresis may result equally from deficiency or surplus of thyroid secretion, and there are other difficulties also.

If enuresis be due to thyroid deficiency, why does it usually occur in the night rather than the day? Surely more demands are made on the activity of the gland during waking hours than in those of sleep? Are we to argue that the gland is therefore exhausted by nightfall, and only by virtue of the night's repose becomes capable of saving the patient from diurnal enuresis also? Or that because rest lessens thyroid activity, therefore in the absence of stimulation engendered by exercise, secretion immediately becomes deficient, and enuresis results?

Such arguments, even if accepted, would only explain the helpful effect of small doses, not the contrary effect of larger doses.

Can it be that the condition is, after all, not directly due to deficiency, but to a temporary excess of thyroid secretion? A condition of thyroidorrhœa, if one may coin such a word. Such thyroidorrhœa (like spermatorrhœa) resulting from and maintaining a relatively exhausted condition of the gland, and therein differing from Graves's disease. Such a condition might readily improve under thyroid medication, but it is easy to see that if enuresis were due to a momentary excess of thyroid secretion in the system, an overdose of the drug would produce a similar result. This hypothesis would explain the beneficial influ-

ence of belladonna, which has probably secured more successes in enuresis than most other drugs have done. I recently had a case of enuresis which proved refractory to thyroid in small or large doses. It was, however, definitely worse on large doses. Accordingly I decided to try aspirin, with the idea that it might neutralize some of the excessive secretion. The immediate result was a dry bed for three nights, an occurrence previously unknown in this case, though the child was 11 years old. The next three or four nights the bed was wetted only once, and then aspirin failed us altogether. The dose given was 5 grains three times a day, and I suppose the explanation is that the child's thyroid, finding more work to do, was stimulated to still greater efforts and an excess of secretion was again produced, with a return of enuresis as the result. One might, of course, suggest an alternative explanation that enuresis was due to deficiency, and the brief respite due to the stimulating effect of aspirin on the thyroid, which, however, soon became still more exhausted and was unable to respond further. In that case, however, a return to thyroid medication should have been successful. But it proved futile. Another point is that this child did not exhibit symptoms of thyroid deficiency in any very marked degree. She was well grown, not unduly sen-

sitive to cold and had a big appetite. Her teeth were very fair, tonsils not enlarged and she had free nasal respiration, though some small adenoids might have been present. She had a high palatine arch and always looked puffy under the eyes, but on the whole general health was good and I could find no other defect. She was not suffering from worms, and her bowels were not constipated.

It has not been my experience that the most marked cases of thyroid deficiency commonly suffer from enuresis, though the victims of enuresis very commonly do exhibit one or more other signs of thyroid inadequacy, and have usually proved amenable to small doses of thyroid as suggested by Leonard Williams. The small doses may act by inhibition, checking excessive thyroid activity, but perhaps it is more likely that they alleviate and so restore to a healthy balance the secretions of the patient's own gland.

In such cases, of course, there might be some advantage to be gained by stirring into activity the patient's own gland with such drugs as arsenic, iodine and calcium, provided the gland were able to respond, and I find iodide of iron among the remedies for enuresis mentioned by Sir Lauder Brunton. There is another matter which needs caution, and that is the preparation of thyroid which is used.

There are probably some on the market which are inactive. It is only natural that the properties and activity of the gland should vary in different animals, according to their age and sex, and probably even according to their pasturage.

Reference has already been made to goitrous sheep and cretin lambs living in districts where the vegetation is deficient in iodine. Accordingly, some thyroids are certainly unsuitable for medical use, and I am informed that experts in this particular branch are able to select the good and reject the bad, which selection might well prove difficult to the uninitiated. The proper percentage of iodine is at least ·2, which should be present in natural condition. I would have nothing to do with preparations containing added iodine. As to the mode of dispensing: the drug may be given of course in tabloid form, or what is more convenient, the requisite amount may be ground up in a mortar with water and incorporated in the mixture, which may contain any other drugs indicated. If desiccated thyroid be used for this purpose, due attention must be given to the fact that it is five times as strong as the ordinary tablet form. This is not expensive for those who dispense their own medicine, the cost of the small doses becoming almost infinitesimal. "Shake the bottle" is

a necessary adjunct, and the mixture must not contain pepsin. I was astonished at the amount of colloid produced by the addition of pepsin to a bottle containing $2\frac{1}{2}$ gr. of desiccated thyroid. The substance thus formed adequately demonstrates the true meaning of the word. The incorporation of the substance in the medicine has many obvious advantages, doing away with any explanation as to what "the little tablets" are for, or as to why they should also be given to other members of the household whose cases may be widely different in other respects. It is perhaps well to add that success in this form of treatment is far more likely to be gained by those who keep careful, if brief, notes of their cases, special attention being paid to such symptoms as pulse-rate, headache, sensation of being hot or cold, regularity of bowels, and weight. If the indications and dose have been correctly gauged the patient will speedily come with assertions of amelioration. The mother will find the child easier to feed and in every way more amenable, and the adult will feel much brighter and less fatigued. Naturally there are many cases in whom this line of treatment is contra-indicated, but the pathological cases are not nearly so common as the thyroid deficients. Many of course are in the pink of health and do not come into this category, but

some cases of thyroid excess which do not amount to Graves's disease will be found among those individuals who are almost fresh-air maniacs, and only feel really well in winter. Such people constantly find the fire too big, perspire easily, and are apt to feel very limp in summer. They dislike fat, and often prefer jam and other sweets to butter. They never need aperients, and are often energetic, and sometimes excitable and impulsive. And if they happen to reside in the same house as the victims of thyroid deficiency, the contrast is most interesting to observe. But this is a subject whose realms may well be further explored, and I fancy that not a few examples will be found among neurasthenics, and possibly also in lunatic asylums.